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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA

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 NEWS 41   May 19  RAPRA enhanced with new search field, simultaneous left and
                   right truncation
 NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43   Jun 06  PASCAL enhanced with additional data

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 12:03:41 ON 13 JUN 2003

=> file reg
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.21       0.21

FILE 'REGISTRY' ENTERED AT 12:03:57 ON 13 JUN 2003
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STRUCTURE FILE UPDATES:   11 JUN 2003  HIGHEST RN 529474-19-9
DICTIONARY FILE UPDATES:  11 JUN 2003  HIGHEST RN 529474-19-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09868276.3
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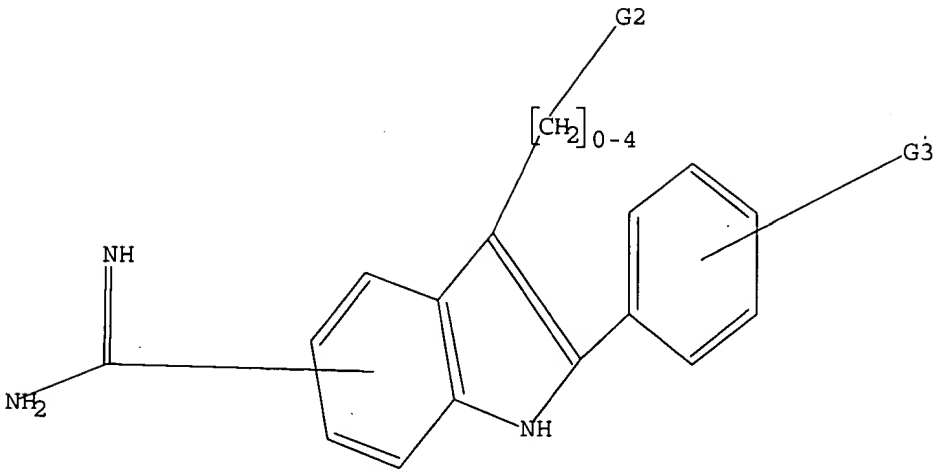
L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1

G2 C,H,Cb,Ak,Cy

G3 X,CH2,OH,PhO,COOH,NH,NH2,P

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 12:05:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 61 TO ITERATE

100.0% PROCESSED 61 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 752 TO 1688
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:05:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1062 TO ITERATE

100.0% PROCESSED 1062 ITERATIONS 119 ANSWERS
SEARCH TIME: 00.00.02

L3 119 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST 148.55 148.76

FILE 'CAPLUS' ENTERED AT 12:05:23 ON 13 JUN 2003
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FILE COVERS 1907 - 13 Jun 2003 VOL 138 ISS 25
FILE LAST UPDATED: 12 Jun 2003 (20030612/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 19 L3

=> d l4 fbib hitstr abs total

L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2003:58259 CAPLUS
DN 138:117652
TI 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid derivatives as factor VIIa inhibitors
IN Hu, Huiyong; Kolesnikov, Aleksandr; Sperandio, David; Young, Wendy Beth; Shrader, William Dvorak
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006670	A2	20030123	WO 2002-US21340	20020703
	WO 2003006670	A3	20030522		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2001-303953PP 20010709
US 2002-351054PP 20020122

PATENT FAMILY INFORMATION:

FAN 2003:57897

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003006011	A1	20030123	WO 2002-US21334	20020703

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

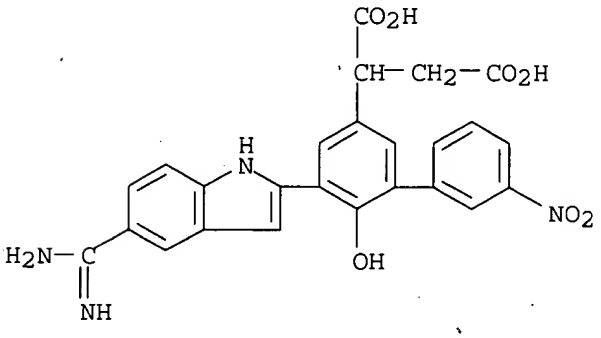
US 2001-303953PP 20010709
US 2002-351054PP 20020122

OS MARPAT 138:117652

IT **488713-56-0P 488713-61-7P 488791-84-0P 488792-03-6P 488792-04-7P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of succinic acid derivs. as anticoagulants)

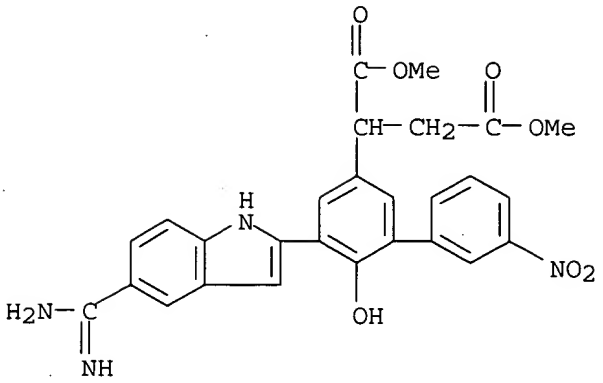
RN 488713-56-0 CAPLUS

CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

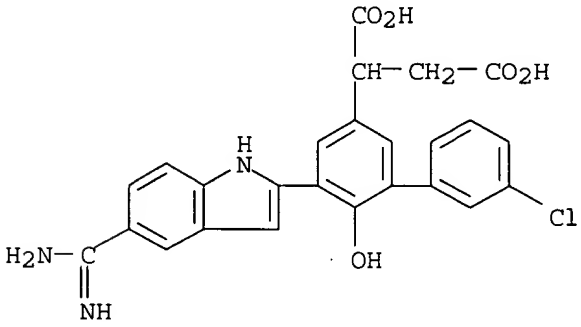


RN 488713-61-7 CAPLUS

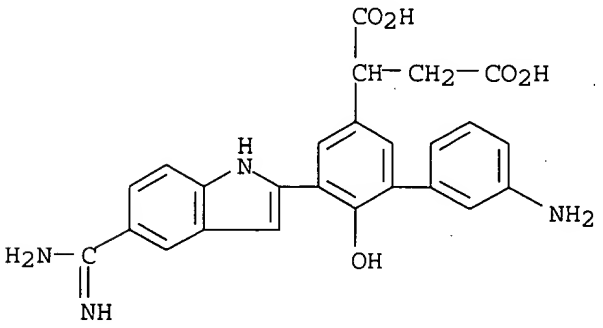
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]-, dimethyl ester (9CI) (CA INDEX NAME)



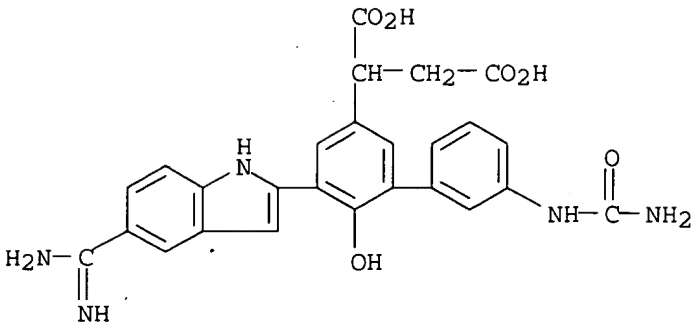
RN 488791-84-0 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-3'-chloro-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488792-03-6 CAPLUS
CN Butanedioic acid, [3'-amino-5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488792-04-7 CAPLUS
CN Butanedioic acid, [3'-[(aminocarbonyl)amino]-5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



AB The present invention relates to derivs. of 2-[5-(5-carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]succinic acid as inhibitors of Factors VIIa, IXa, Xa, XIa, in particular Factor VIIa, pharmaceutical compns. comprising these inhibitors, and methods for using these inhibitors for treating or preventing thromboembolic disorders. For example, 2-[5-(5-carbamimidoyl-1H-benzoimidazol-2-yl)-6-hydroxy-3'-nitro-biphenyl-3-yl]-succinic acid was prepd. by reaction of 2-(5-formyl-6-hydroxy-3'-nitro-biphenyl-3-yl)-succinic acid (0.3 g) and 3,4-diaminobenzamidine monohydrochloride (0.17 g) in a yield of 63%.

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2003:57897 CAPLUS
DN 138:122645
TI Preparation of 2-[5-(5-Carbamimidoyl-1H-heteroaryl)-6-hydroxybiphenyl-3-yl]-succinic acid derivatives as factor VIIa inhibitors
IN Hu, Huiyong; Kolesnikov, Aleksandr; Rai, Roopa; Shrader, William Dvorak; Young, Wendy Beth; Sperandio, David; Hendrix, John; Torkelson, Steve
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006011	A1	20030123	WO 2002-US21334	20020703
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2001-303953PP	20010709
				US 2002-351054PP	20020122

PATENT FAMILY INFORMATION:
FAN 2003:58259

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006670	A2	20030123	WO 2002-US21340	20020703
	WO 2003006670	A3	20030522		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

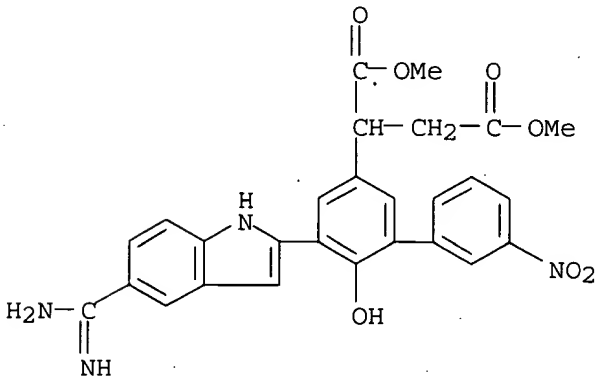
US 2001-303953PP 20010709
US 2002-351054PP 20020122

OS MARPAT 138:122645

IT **488713-61-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of [(carbamimidoyl-1H-heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa inhibitors for treating thromboembolic disorders)

RN 488713-61-7 CAPLUS

CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro[1,1'-biphenyl]-3-yl]-, dimethyl ester (9CI) (CA INDEX NAME)

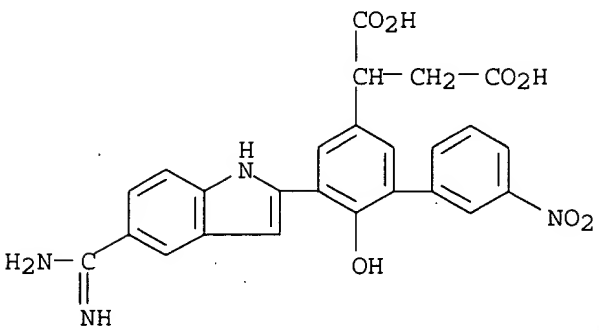


IT **488713-56-0P**, 2-[5-(5-Carbamimidoyl-1H-indol-2-yl)-6-hydroxy-3'-nitrobiphenyl-3-yl]succinic acid **488713-62-8P**, 2-[5-(5-Carbamimidoyl-1H-indol-2-yl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid **488713-63-9P**, 2-[5-(5-Carbamimidoyl-6-chloro-1H-indol-2-yl)-6,2'-dihydroxybiphenyl-3-yl]succinic acid **488713-64-0P**, (E)-2-[5-(5-Carbamimidoyl-1H-indol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]but-2-enedioic acid **488713-65-1P**, (Z)-2-[5-(5-Carbamimidoyl-1H-indol-2-yl)-5'-fluoro-6,2'-dihydroxybiphenyl-3-yl]but-2-enedioic acid **488713-77-5P**, 2-[5-(5-Carbamimidoyl-1H-indol-2-yl)-2',6-dihydroxy-5'-aminocarbonylbiphenyl-3-yl]succinic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(carbamimidoyl-1H-heteroaryl)hydroxybiphenylyl]succinic acid derivs. as factor VIIa inhibitors for treating thromboembolic disorders)

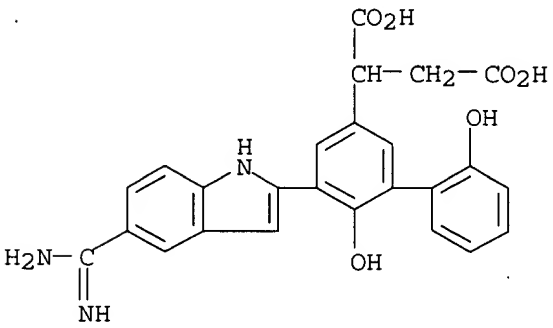
RN 488713-56-0 CAPLUS

CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-

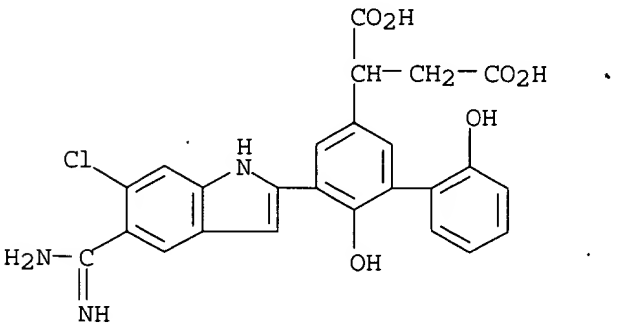
nitro[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 488713-62-8 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-1H-indol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

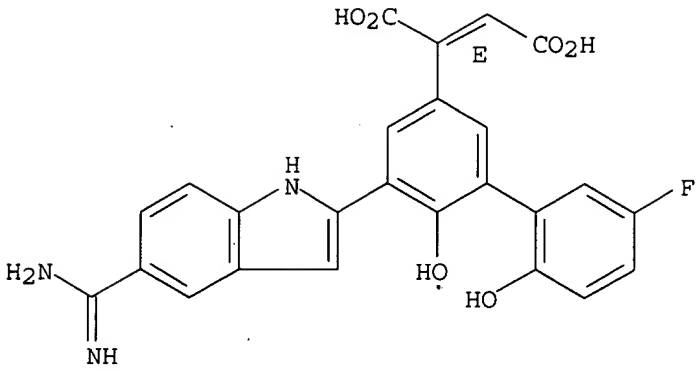


RN 488713-63-9 CAPLUS
CN Butanedioic acid, [5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-2',6-dihydroxy[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



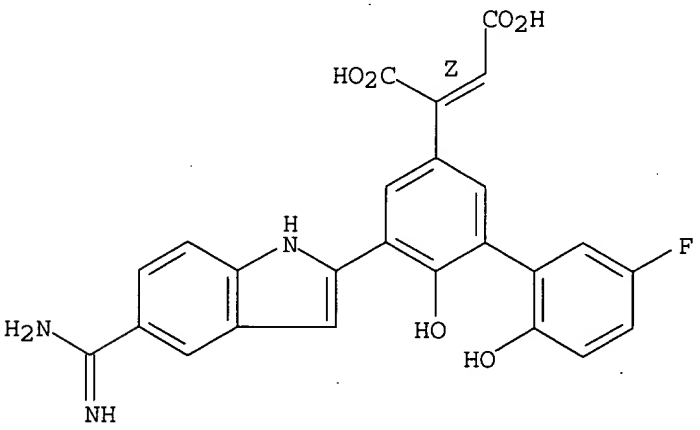
RN 488713-64-0 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-indol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, (2E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 488713-65-1 CAPLUS
CN 2-Butenedioic acid, 2-[5-[5-(aminoiminomethyl)-1H-indol-2-yl]-5'-fluoro-2',6-dihydroxy[1,1'-biphenyl]-3-yl]-, (2Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 488713-77-5 CAPLUS
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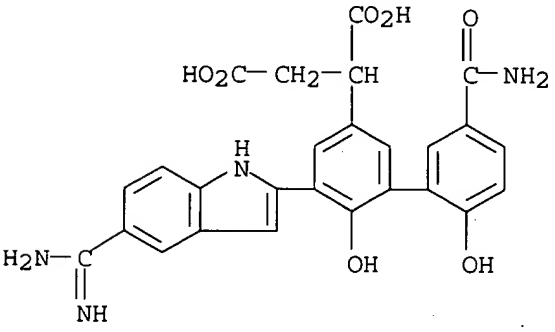
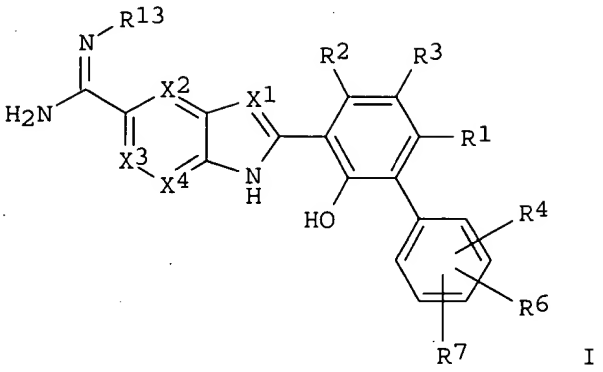


GI



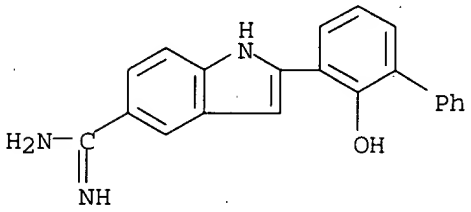
I

AB The present invention relates to [I; X1-X4 = N, CR5 (wherein R5 = H, alkyl); provided that not more than three of X1-X4 are N; R1, R2 = H, alkyl, halo; R3 = CO2R9, -(alkylene)-CO2R9, CR8(CO2R11)alkylene-CO2R9, -C(R8)[(alkylene)nCO2R9]CH(R10)CO2R11 (wherein R8 = H, alkyl, HO; R10 = H, alkyl; R8 and R10 together forms a covalent bond; R9, R11 = H, alkyl, haloalkyl, aryl, aralkyl); R4 = H, alkyl, alkylthio, halo, HO, hydroxyalkyl, alkoxy, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, NO2; R6 = H, alkyl, halo; R7 = H, alkyl, cycloalkyl, alkylthio, halo, HO, NO2, cyano, alkoxy, haloalkoxy, CO2H, alkoxycarbonyl, acylamino, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, etc.; R13 = H, HO, C1-10 alkoxy, COR35 (wherein R35 = alkyl, aryl, haloalkyl, cyanoalkyl, alkoxycarbonyl, hydroxyalkoxycarbonyl, acyloxycarbonyl, haloalkoxycarbonyl)] and individual isomers, mixts. of isomers, or pharmaceutically acceptable salts thereof which are novel inhibitors of factors VIIa, IXa, Xa, XIa, in particular factor VIIa (no data). Also disclosed are pharmaceutical compns. contg. the compds. I for treating or preventing a disease mediated by factor VIIa, in particular thromboembolic disorders. Also claimed is a method for inhibiting coagulation of a biol. sample. Thus, A mixt. of 0.3 g 2-(5-formyl-6-hydroxy-3'-nitrobiphenyl-3-yl)succinic acid, 0.17 g, 3,4-diaminobenzamidine monohydrochloride, and 0.097 g benzoquinone in 50 mL ethanol was heated for approx. 4 h to give, after purifn. by reverse phase HPLC (gradient, acetonitrile/0.02 N aq. HCl) to give 63% 2-[5-(5-carbamimidoyl-1H-benzimidazol-2-yl)-6-hydroxy-3'-nitrobiphenyl-3-yl]succinic acid.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:680206 CAPLUS
DN 137:365440
TI Contribution of Multicentered Short Hydrogen Bond Arrays to Potency of Active Site-Directed Serine Protease Inhibitors
AU Katz, Bradley A.; Spencer, Jeffrey R.; Elrod, Kyle; Luong, Christine; Mackman, Richard L.; Rice, Mark; Sprengeler, Paul A.; Allen, Darin; Janc, James
CS Celera, South San Francisco, CA, 94080, USA
SO Journal of the American Chemical Society (2002), 124(39), 11657-11668
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society

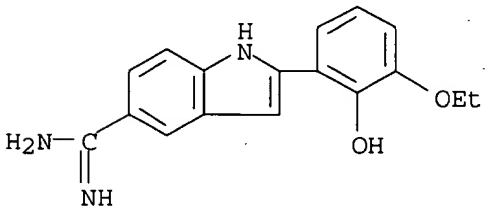
DT Journal
LA English
IT **277312-42-2D**, CRA 8696, complexes with enzymes
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(multicentered short hydrogen bond arrays may contribute to potency of active site-directed serine protease inhibitors)
RN 277312-42-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



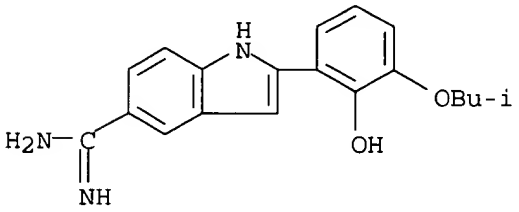
AB We describe and compare the pH dependencies of the potencies and of the bound structures of two inhibitor isosteres that form multicentered short hydrogen bond arrays at the active sites of trypsin, thrombin, and urokinase type plasminogen activator (urokinase or uPA) over certain ranges of pH. Depending on the pH, short hydrogen bond arrays at the active site are mediated by two waters, one in the oxyanion hole (H2Ooxy) and one on the other (S2) side of the inhibitor (H2OS2), by one water (H2Ooxy), or by no water. The dramatic variation in the length of the active site hydrogen bonds as a function of pH, of inhibitor, and of enzyme, along with the involvement or absence of ordered water, produces a large structural manifold of active site hydrogen bond motifs. Diverse examples of multicentered and two-centered short hydrogen bond arrays, both at and away from the active site, recently discovered in several protein crystal systems, suggest that short hydrogen bonds in proteins may be more common than has been recognized. The short hydrogen bond arrays resemble one another with respect to ionic nature, highly polar environment, multitude of assocd. ordinary hydrogen bonds, and disparate pKa values of participating groups. Comparison of structures and Ki values of trypsin complexes at pH values where the multicentered short hydrogen bond arrays mediating inhibitor binding are present or absent indicate that these arrays have a minor effect on inhibitor potency. These features suggest little covalent nature within the short hydrogen bonds, despite their extraordinary shortness (as short as 2.0 .ANG.).
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:510523 CAPLUS
DN 138:162956
TI 2-(2-Hydroxy-3-alkoxyphenyl)-1H-benzimidazole-5-carboxamidine derivatives as potent and selective urokinase-type plasminogen activator inhibitors
AU Mackman, Richard L.; Hui, Hon C.; Breitenbucher, J. Guy; Katz, Bradley A.; Luong, Christine; Martelli, Arnold; McGee, Danny; Radika, Kesavan; Sendzik, Martin; Spencer, Jeffrey R.; Sprengeler, Paul A.; Tario, James; Verner, Erik; Wang, Jing
CS Celera, South San Francisco, CA, 94080, USA
SO Bioorganic & Medicinal Chemistry Letters (2002), 12(15), 2019-2022

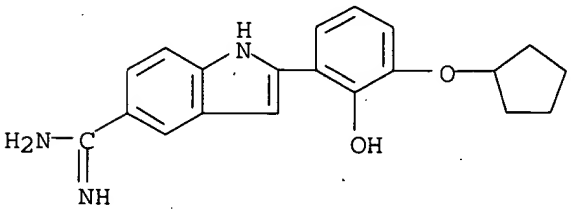
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 138:162956
IT **497147-73-6P 497147-74-7P 497147-75-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug design for potent and selective urokinase-type plasminogen activator inhibitors)
RN 497147-73-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-ethoxy-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 497147-74-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-3-(2-methylpropoxy)phenyl]- (9CI) (CA INDEX NAME)

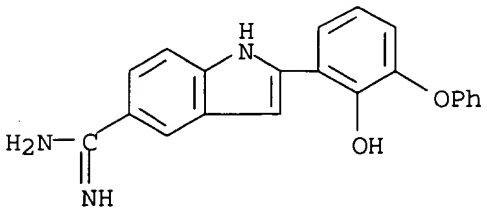


RN 497147-75-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[3-(cyclopentyloxy)-2-hydroxyphenyl]- (9CI) (CA INDEX NAME)



IT **497147-72-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug design for potent and selective urokinase-type plasminogen activator inhibitors)

RN 497147-72-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-3-phenoxyphenyl)- (9CI) (CA INDEX NAME)



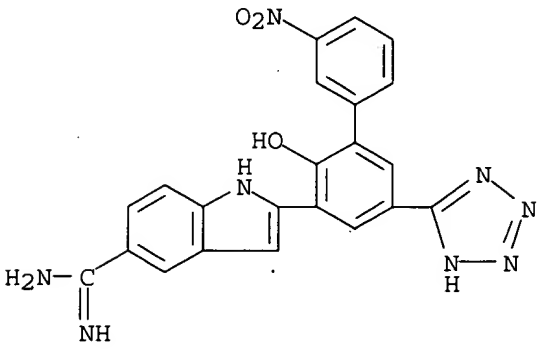
AB The development of potent and selective urokinase-type plasminogen activator (uPA) inhibitors based on the lead mol. 2-(2-hydroxy-3-ethoxyphenyl)-1H-benzimidazole-5-carboxamidine is described.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:142700 CAPLUS
DN 136:183829
TI Preparation of azolylbiphenylylindolecarboxamidines Factor VIIa inhibitors
IN Leahy, Ellen M.
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

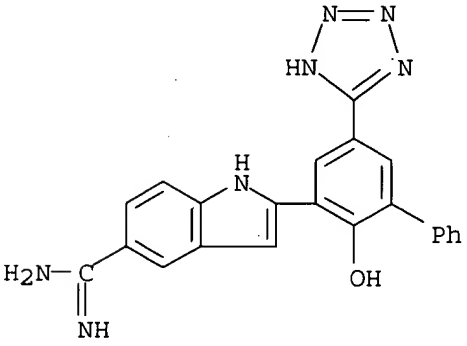
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002014307	A1	20020221	WO 2001-US25324	20010811
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			US 2000-224713PP	20000811
US 2002037912	A1	20020328	US 2001-927423	20010810
			US 2000-224713PP	20000811
AU 2001083340	A5	20020225	AU 2001-83340	20010811
			US 2000-224713PP	20000811
			WO 2001-US25324W	20010811

OS MARPAT 136:183829
IT **381210-39-5P 400008-32-4P 400008-33-5P**
400008-34-6P 400008-35-7P 400008-36-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azolylbiphenylylindolecarboxamidines as Factor VIIa inhibitors)
RN 381210-39-5 CAPLUS

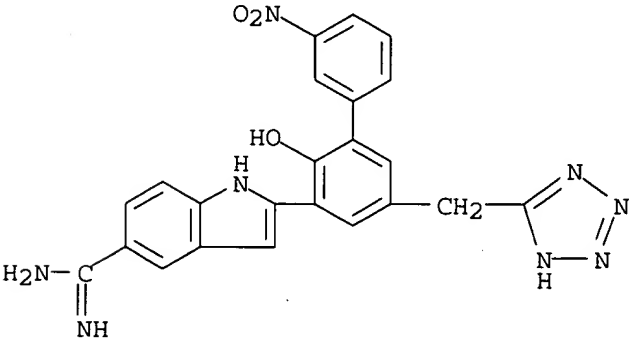
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-3'-nitro-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 400008-32-4 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

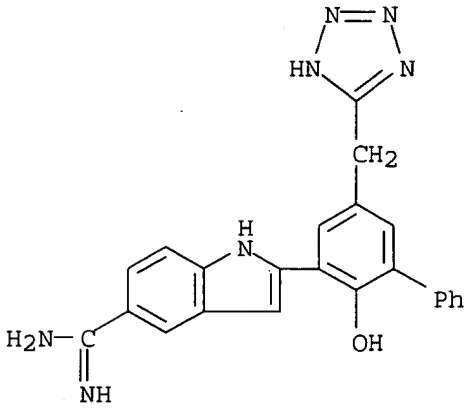


RN 400008-33-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-3'-nitro-5-(1H-tetrazol-5-ylmethyl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)

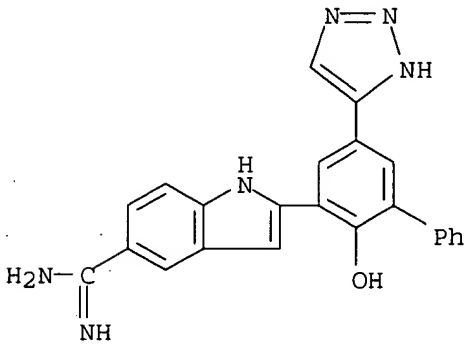


RN 400008-34-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-5-(1H-tetrazol-5-ylmethyl)[1,1'-

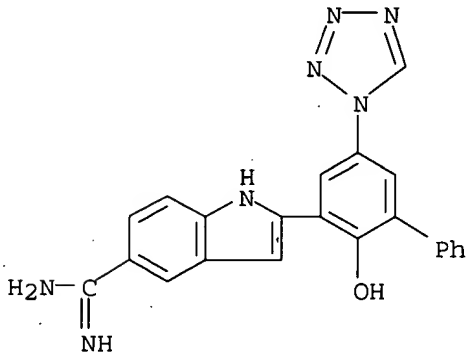
biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 400008-35-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-5-(1H-1,2,3-triazol-4-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 400008-36-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-5-(1H-tetrazol-1-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



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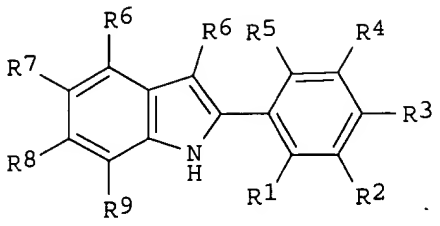


I

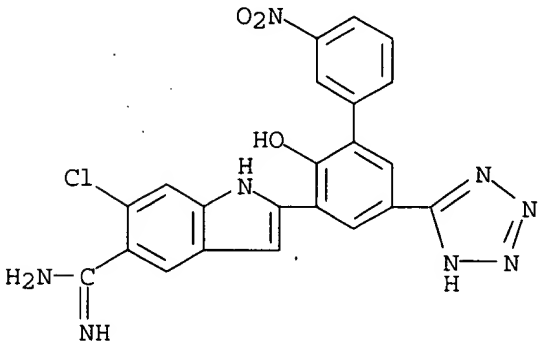
AB Title compds. [I; R1 = OH; R2 = Ph, nitrophenyl; R3, R5, R8, R9 = H; R4 = (CH2)0-2-tetrazolyl, (CH2)0-2-triazolyl; R6 = H, CH2Ph; R7 = amino, amidino, guanidino], were prepd. as antithrombotics (no data). 1-[3-Bromo-2-hydroxy-5-(1H-tetrazol-5-yl)phenyl]ethanone, 3-nitrophenylboronic acid, Na2CO3, and Pd(PPh3)4 were refluxed 8-16 h in EtOH/PhMe/H2O to give 100% 1-[2-hydroxy-3-nitro-5-(1H-tetrazol-5-yl)biphenyl-3-yl]ethanone. The latter was refluxed with 4-hydrazinobenzamidine and diisopropylethylamine in EtOH for 8-16 h to give a hydrazone which was heated in polyphosphoric acid at 165.degree. for 1 h to give 3% 2-[2-hydroxy-3-nitro-5-(1H-tetrazol-5-yl)biphenyl-3-yl]-1H-indole-5-carboxamidine.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

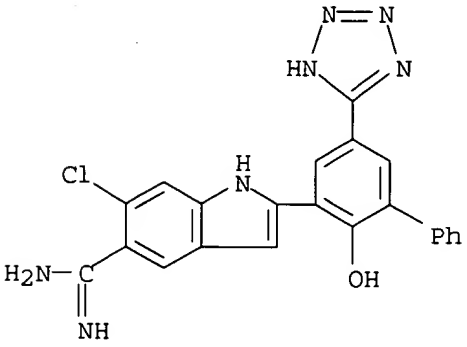
L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2002:142669 CAPLUS
DN 136:200191
TI Preparation of 2-(3-tetrazolyl or 3-triazolylphenyl)indoles as selective urokinase inhibitors
IN Mackman, Richard L.
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014274	A1	20020221	WO 2001-US25315	20010811
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				US 2000-224712PP	20000811
	US 2002045650	A1	20020418	US 2001-927785	20010810
	US 6465503	B2	20021015		
				US 2000-224712PP	20000811
	AU 2001083336	A5	20020225	AU 2001-83336	20010811
				US 2000-224712PP	20000811
				WO 2001-US25315W	20010811

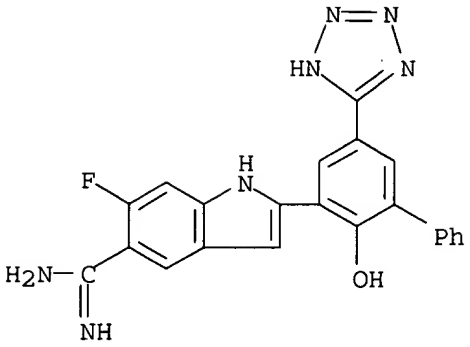
OS MARPAT 136:200191
IT **400781-28-4P 400781-29-5P 400781-30-8P**
400781-31-9P 400781-32-0P 400781-33-1P
400781-34-2P 400781-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-(3-tetrazolyl or 3-triazolylphenyl)indoles as selective urokinase inhibitors)
RN 400781-28-4 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-[2-hydroxy-3'-nitro-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



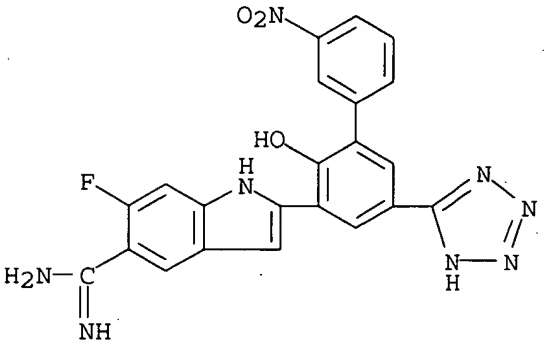
RN 400781-29-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-[2-hydroxy-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



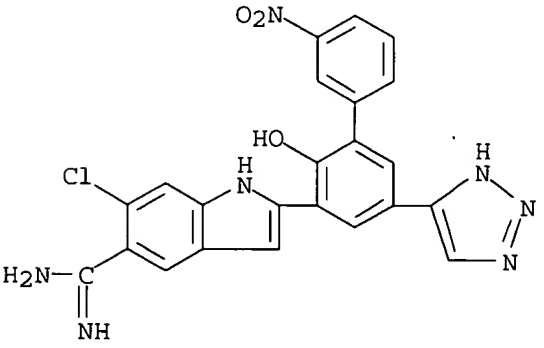
RN 400781-30-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-[2-hydroxy-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



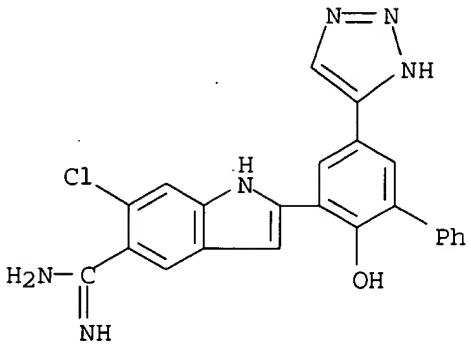
RN 400781-31-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-[2-hydroxy-3'-nitro-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



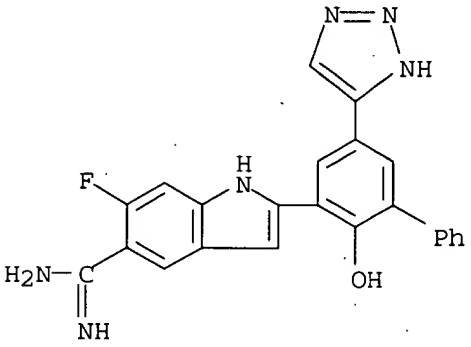
RN 400781-32-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-[2-hydroxy-3'-nitro-5-(1H-1,2,3-triazol-4-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



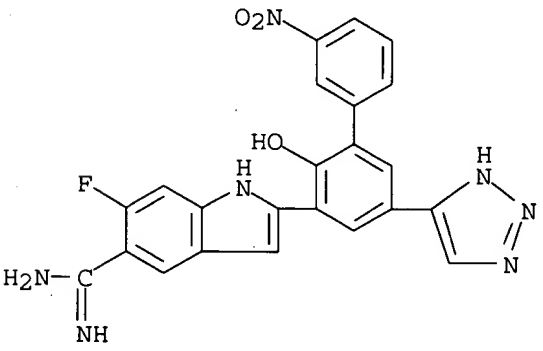
RN 400781-33-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-[2-hydroxy-5-(1H-1,2,3-triazol-4-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



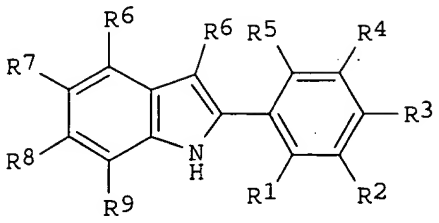
RN 400781-34-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-[2-hydroxy-5-(1H-1,2,3-triazol-4-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



RN 400781-35-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-[2-hydroxy-3'-nitro-5-(1H-1,2,3-triazol-4-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



GI

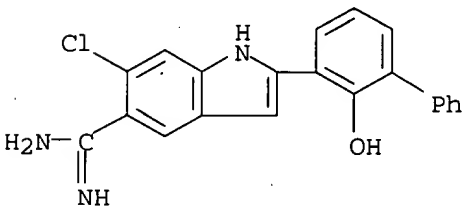


I

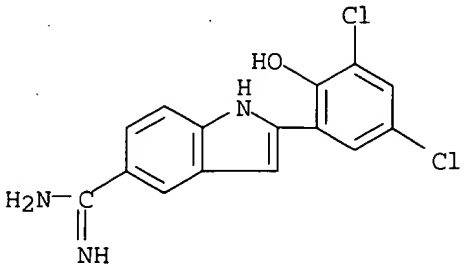
AB The title compds. [I; R1 = OH; R2 = Ph, nitrophenyl; R3 = H; R4 = (CH2)0-2tetrazolyl, (CH2)0-2triazolyl; R5 = H; R6 = H; R7 = NH2, amidino, guanidino; R8 = halo; R9 = H] which are inhibitors of uPA (no data), and have utility as cancer treating agents, were prepd. E.g., a 3-step synthesis of I [R1 = OH: 3-NO2C6H4; R3 = H; R4 = 1H-tetrazol-5-yl; R5, R6 = H; R7 = C(:NH)NH2; R8 = Cl; R9 = H], starting with 1-[3-bromo-2-hydroxy-5-(1H-tetrazol-5-yl)phenyl]ethanone, was given.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

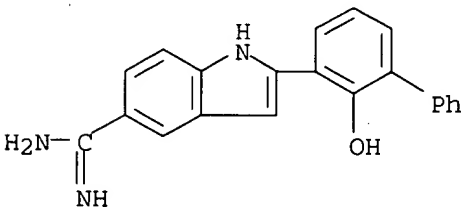
L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:866569 CAPLUS
DN 136:395308
TI Engineering inhibitors highly selective for the S1 sites of Ser190 trypsin-like serine protease drug targets
AU Katz, Bradley A.; Sprengeler, Paul A.; Luong, Christine; Verner, Erik; Elrod, Kyle; Kirtley, Matt; Janc, James; Spencer, Jeffrey R.; Breitenbucher, J. Guy; Hui, Hon; McGee, Danny; Allen, Darin; Martelli, Arnold; Mackman, Richard L.
CS Axys Pharmaceutical Corporation, South San Francisco, CA, 94080, USA
SO Chemistry & Biology (2001), 8(11), 1107-1121
CODEN: CBOLE2; ISSN: 1074-5521
PB Elsevier Science Ltd.
DT Journal
LA English
IT **277312-21-7**, APC 10302 **277312-33-1**, APC 9008
277312-42-2, APC 8696 **277312-54-6**, APC 9850
277312-62-6, APC 11417
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(APC-7806 (benzimidazole) and APC-8696 (indole) series inhibitors highly selective for S1 sites of Ser190 trypsin-like serine protease drug targets and their structure-activity relationship)
RN 277312-21-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



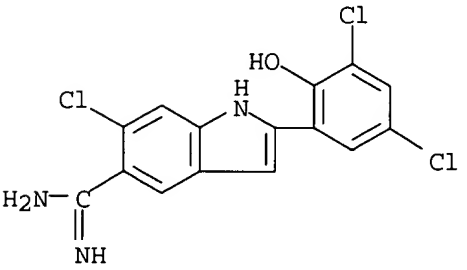
RN 277312-33-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dichloro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



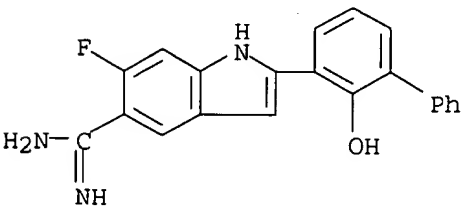
RN 277312-42-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)

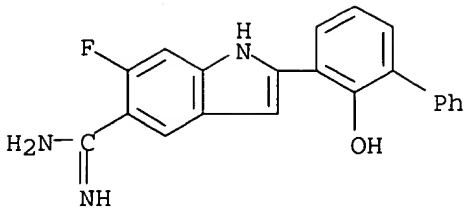


RN 277312-54-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-(3,5-dichloro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 277312-62-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)





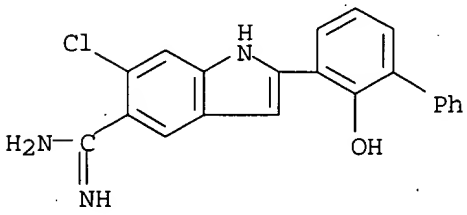
AB Background: Involved or implicated in a wide spectrum of diseases, trypsin-like serine proteases comprise well studied drug targets and anti-targets that can be subdivided into two major classes. In one class there is a serine at position 190 at the S1 site, as in urokinase type plasminogen activator (urokinase or uPA) and factor VIIa, and in the other there is an alanine at 190, as in tissue type plasminogen activator (tPA) and factor Xa. A hydrogen bond unique to Ser190 protease-arylamidine complexes between O.gamma.Ser190 and the inhibitor amidine confers an intrinsic preference for such inhibitors toward Ser190 proteases over Ala190 counterparts. Results: Based on the structural differences between the S1 sites of Ser190 and Ala190 protease-arylamidine complexes, we amplified the selectivity of amidine inhibitors toward uPA and against tPA, by factors as high as 220-fold, by incorporating a halo group ortho to the amidine of a lead inhibitor scaffold. Comparison of Ki values of such halo-substituted and parent inhibitors toward a panel of Ser190 and Ala190 proteases demonstrates pronounced selectivity of the halo analogs for Ser190 proteases over Ala190 counterparts. Crystal structures of Ser190 proteases, uPA and trypsin, and of an Ala190 counterpart, thrombin, bound by a set of ortho (halo, amidino) aryl inhibitors and of non-halo parents reveal the structural basis of the exquisite selectivity and validate the design principle. Conclusions: Remarkable selectivity enhancements of exceptionally small inhibitors are achieved toward the uPA target over the highly similar tPA anti-target through a single atom substitution on an otherwise relatively non-selective scaffold. Overall selectivities for uPA over tPA as high as 980-fold at physiol. pH were realized. The increase in selectivity results from the displacement of a single bound water mol. common to the S1 site of both the uPA target and the tPA anti-target because of the ensuing deficit in hydrogen bonding of the arylamidine inhibitor when bound in the Ala190 protease anti-target.

RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:731858 CAPLUS
DN 136:31297
TI Exploiting Subsite S1 of Trypsin-Like Serine Proteases for Selectivity: Potent and Selective Inhibitors of Urokinase-Type Plasminogen Activator
AU Mackman, Richard L.; Katz, Bradley A.; Breitenbucher, J. Guy; Hui, Hon C.; Verner, Erik; Luong, Christine; Liu, Liang; Sprengeler, Paul A.
CS Departments of Medicinal Chemistry Structural Biology and Preclinical Sciences, Axys Pharmaceuticals Inc., South San Francisco, CA, 94080, USA
SO Journal of Medicinal Chemistry (2001), 44(23), 3856-3871
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **277312-21-7P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU

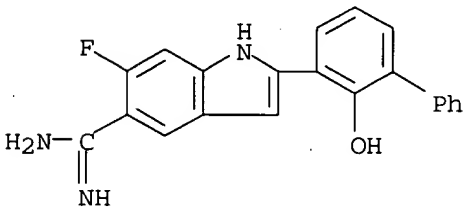
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(exploiting subsite S1 of trypsin-like serine proteases for selectivity to design potent and selective inhibitors of urokinase-type plasminogen activators in relation to pharmacokinetics)

RN 277312-21-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)

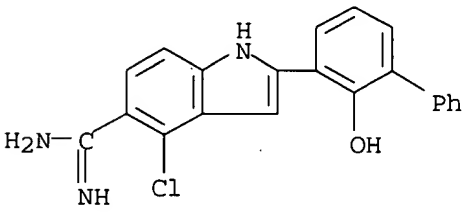


IT **277312-62-6P 380241-57-6P 380241-87-2P 380241-89-4P**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(exploiting subsite S1 of trypsin-like serine proteases for selectivity to design potent and selective inhibitors of urokinase-type plasminogen activators in relation to pharmacokinetics)

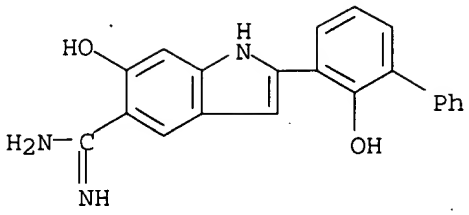
RN 277312-62-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



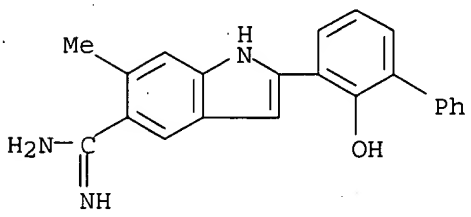
RN 380241-57-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 4-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



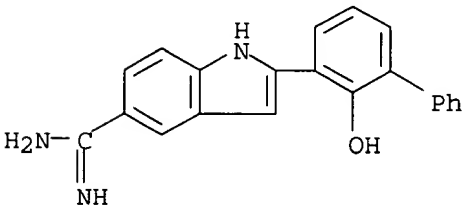
RN 380241-87-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-hydroxy-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



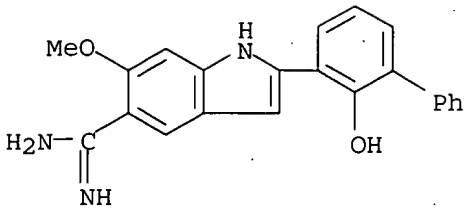
RN 380241-89-4 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)-6-methyl- (9CI) (CA INDEX NAME)



IT **277312-42-2**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(exploiting subsite S1 of trypsin-like serine proteases for selectivity to design potent and selective inhibitors of urokinase-type plasminogen activators in relation to pharmacokinetics)
RN 277312-42-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



IT **380241-85-0P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(exploiting subsite S1 of trypsin-like serine proteases for selectivity to design potent and selective inhibitors of urokinase-type plasminogen activators in relation to pharmacokinetics)
RN 380241-85-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)-6-methoxy- (9CI) (CA INDEX NAME)



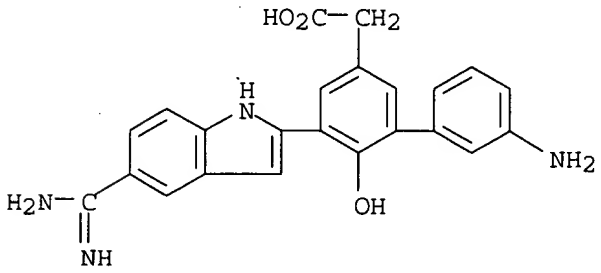
AB A nonselective inhibitor of trypsin-like serine proteases, 2-(2-hydroxybiphenyl-3-yl)-1H-indole-5-carboxamidine (I) (Verner, E.; Katz, B. A.; Spencer, J.; Allen, D.; Hataye, J.; Hruzewicz, W.; Hui, H. C.; Kolesnikov, A.; Li, Y.; Luong, C.; Martelli, A.; Radika. K.; Rai, R.; She, M.; Shrader, W.; Sprengeler, P. A.; Trapp, S.; Wang, J.; Young, W. B.; Mackman, R. L. J. Med. Chem. 2001, 44, 2753-2771) has been optimized through minor structural changes on the S1 binding group to afford remarkably selective and potent inhibitors of urokinase-type plasminogen activator (uPA). The trypsin-like serine proteases1 that comprise drug targets can be broadly categorized into two subfamilies, those with Ser190 and those with Ala190. A single-atom modification, for example, replacement of hydrogen for chlorine at the 6-position of the 5-amidinoindole P1 group on I, generated .ltoreq.6700-fold selectivity toward the Ser190 enzymes and against the Ala190 enzymes. The larger chlorine atom displaces a water mol. (H2O1S1) that binds near residue 190 in all the complexes of I, and related inhibitors, in uPA, thrombin, and trypsin. The water mol., H2O1S1, in both the Ser190 or Ala190 enzymes, hydrogen bonds with the amidine N1 nitrogen of the inhibitor. When it is displaced, a redn. in affinity toward the Ala190 enzymes is obsd. due to the amidine N1 nitrogen of the bound inhibitor being deprived of a key hydrogen-bonding partner. In the Ser190 enzymes the affinity is maintained since the serine hydroxyl oxygen O.gamma.Ser190 compensates for the displaced water mol. High-resoln. crystallog. provided evidence for the displacement of the water mol. and validated the design rationale. In summation, a novel and powerful method for engineering selectivity toward Ser190 proteases and against Ala190 proteases without substantially increasing mol. wt. is described.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

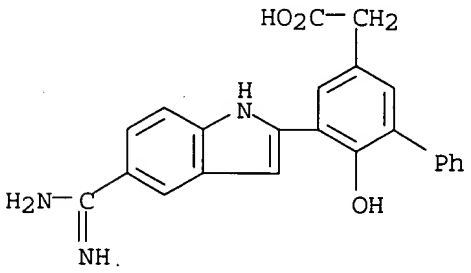
L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:628981 CAPLUS
DN 136:47957
TI Optimization of a screening lead for factor VIIa/TF
AU Young, W. B.; Kolesnikov, A.; Rai, R.; Sprengeler, P. A.; Leahy, E. M.; Shrader, W. D.; Sangalang, J.; Burgess-Henry, J.; Spencer, J.; Elrod, K.; Cregar, L.
CS Departments of Medicinal Chemistry, Structural Chemistry, and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(17), 2253-2256
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
IT **381210-27-1P 381210-28-2P 381210-29-3P**
381210-30-6P 381210-31-7P 381210-32-8P
381210-33-9P 381210-34-0P 381210-35-1P
381210-36-2P 381210-37-3P 381210-38-4P
381210-39-5P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure based design of an indole biphenyl inhibitor of factor VIIa/TF with improved selectivity vs. related enzymes)

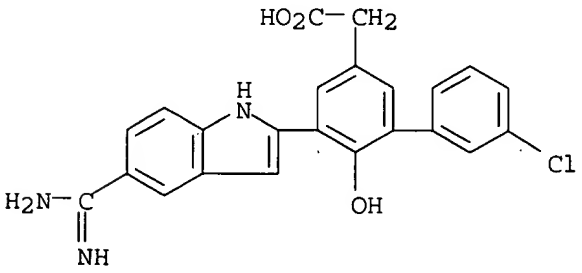
RN 381210-27-1 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 3'-amino-5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy- (9CI) (CA INDEX NAME)



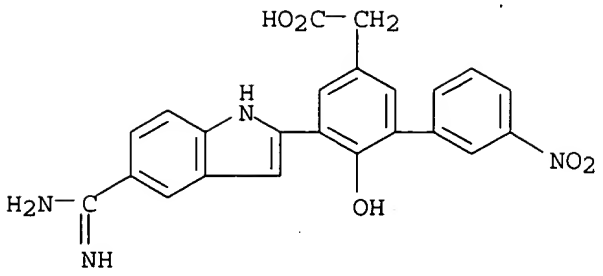
RN 381210-28-2 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy- (9CI) (CA INDEX NAME)



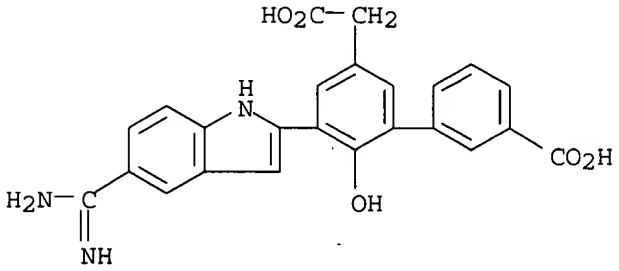
RN 381210-29-3 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-3'-chloro-6-hydroxy- (9CI) (CA INDEX NAME)



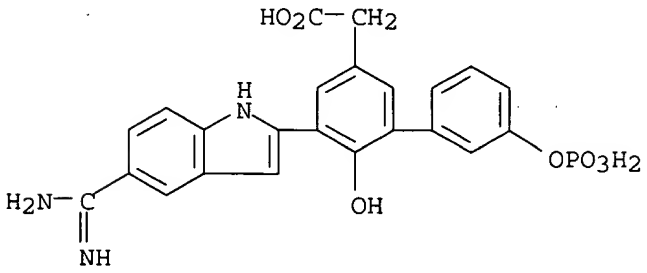
RN 381210-30-6 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro- (9CI) (CA INDEX NAME)



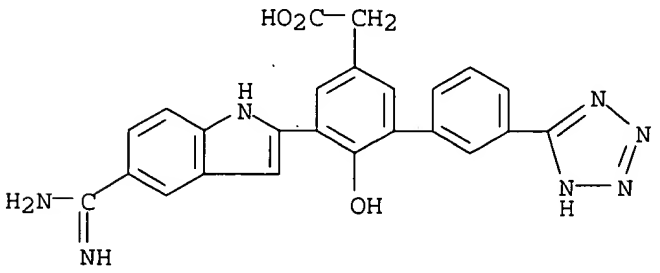
RN 381210-31-7 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-3'-carboxy-6-hydroxy- (9CI) (CA INDEX NAME)



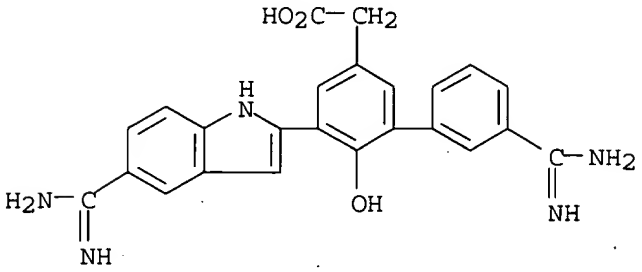
RN 381210-32-8 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-(phosphonooxy)- (9CI) (CA INDEX NAME)



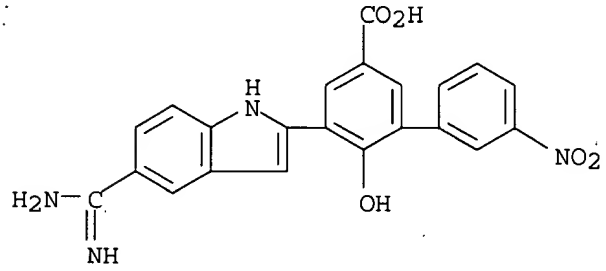
RN 381210-33-9 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-(1H-tetrazol-5-yl)- (9CI) (CA INDEX NAME)



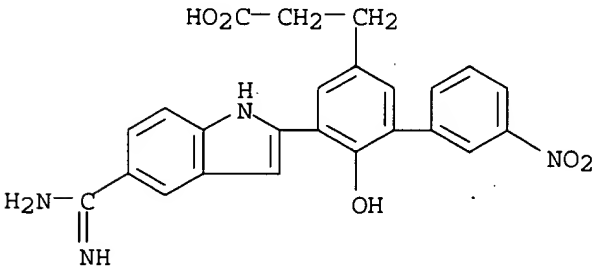
RN 381210-34-0 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 3'-(aminoiminomethyl)-5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy- (9CI) (CA INDEX NAME)



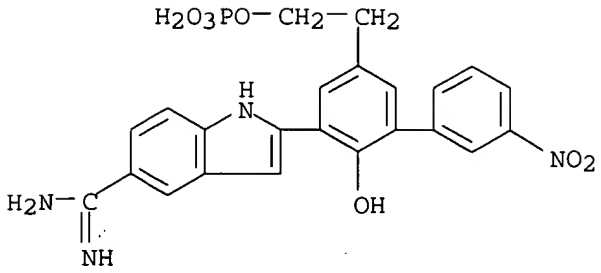
RN 381210-35-1 CAPLUS
CN [1,1'-Biphenyl]-3-carboxylic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro- (9CI) (CA INDEX NAME)



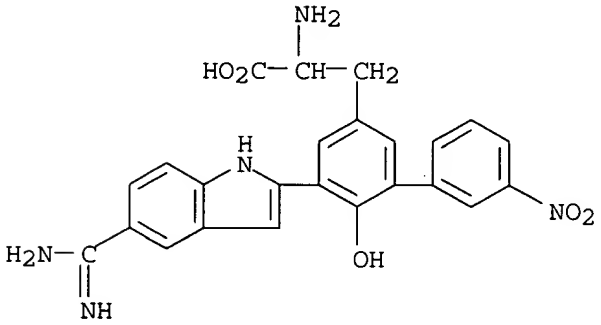
RN 381210-36-2 CAPLUS
CN [1,1'-Biphenyl]-3-propanoic acid, 5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro- (9CI) (CA INDEX NAME)



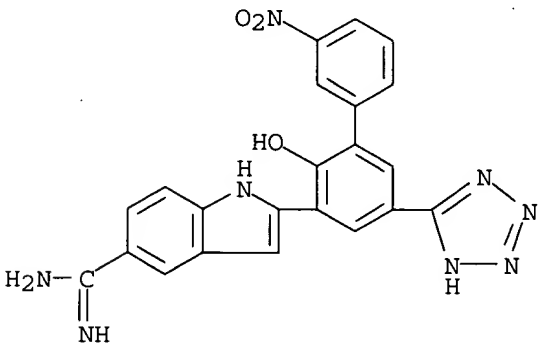
RN 381210-37-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-3'-nitro-5-[2-(phosphonooxy)ethyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



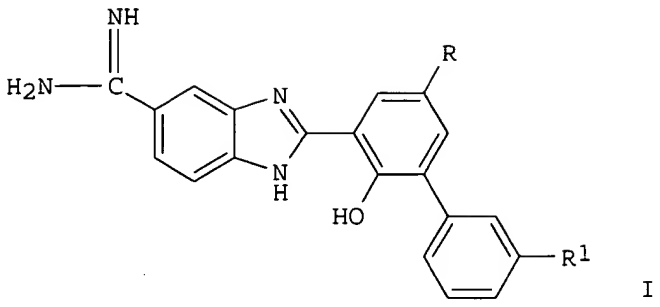
RN 381210-38-4 CAPLUS
CN [1,1'-Biphenyl]-3-propanoic acid, .alpha.-amino-5-[5-(aminoiminomethyl)-1H-indol-2-yl]-6-hydroxy-3'-nitro- (9CI) (CA INDEX NAME)



RN 381210-39-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-3'-nitro-5-(1H-tetrazol-5-yl)[1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



GI

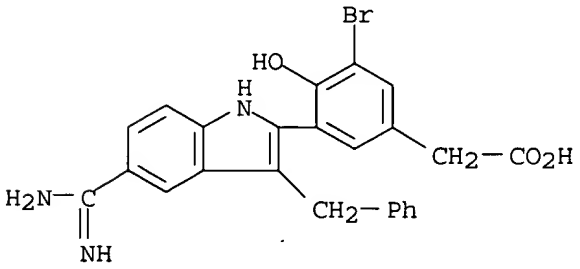


I

AB The structure-based design and progression of a screening lead (I, R = Cl, R1 = NH2) to a 3 nM factor VIIa/TF inhibitor I, (R = CH2CO2H, R1 = NO2) with improved selectivity vs. related enzymes is described.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:518599 CAPLUS
DN 135:313147
TI Development of potent and selective factor Xa inhibitors
AU Rai, R.; Kolesnikov, A.; Li, Y.; Young, W.; Leahy, E.; Sprengeler, P.; Verner, E.; Shrader, W.; Burgess-Henry, J.; Sangalang, J.; Allen, D.; Chen, X.; Katz, B.; Luong, C.; Elrod, K.; Cregar, L.
CS Departments of Medicinal Chemistry, Structural Chemistry and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(14), 1797-1800
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
IT **277312-22-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(development of potent and selective factor Xa inhibitors in relation to inhibition of thrombin)
RN 277312-22-8 CAPLUS
CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)

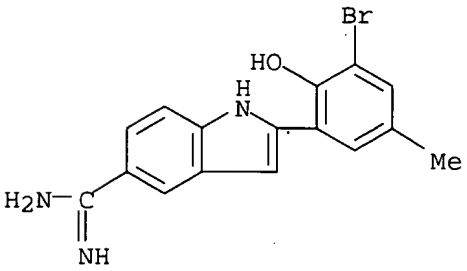


IT **277312-31-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of potent and selective factor Xa inhibitors in relation to inhibition of thrombin)

RN 277312-31-9 CAPLUS

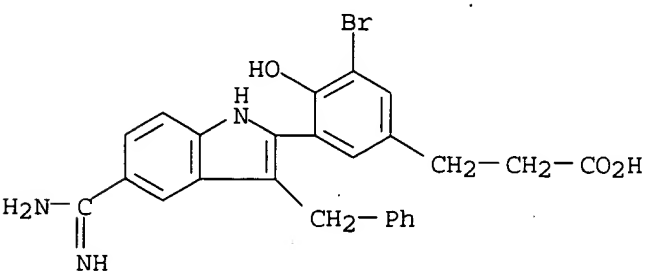
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



IT **277312-23-9P 277312-32-0P 277312-41-1P**
277312-48-8P 277312-51-3P 277312-53-5P
277312-74-0P 277312-82-0P 277312-84-2P
277312-85-3P 277312-86-4P 368878-92-6P
368878-93-7P 368878-94-8P 368878-95-9P
368878-96-0P 368878-97-1P 368878-98-2P
368878-99-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(development of potent and selective factor Xa inhibitors in relation to inhibition of thrombin)

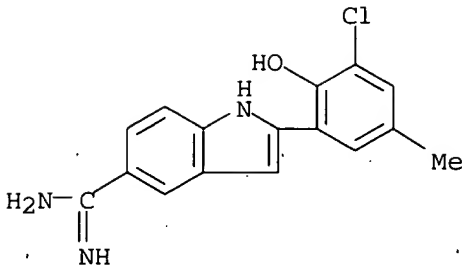
RN 277312-23-9 CAPLUS

CN Benzenepropanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)

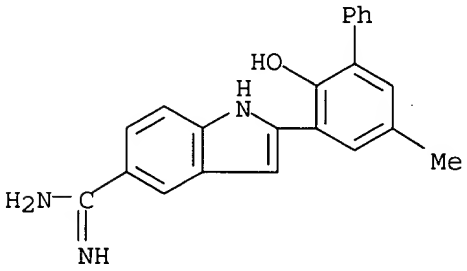


RN 277312-32-0 CAPLUS

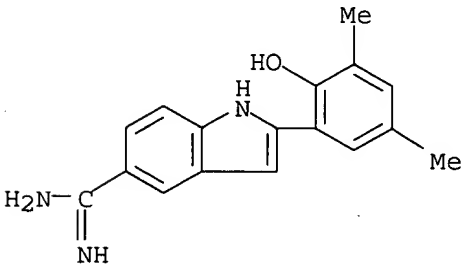
CN 1H-Indole-5-carboximidamide, 2-(3-chloro-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



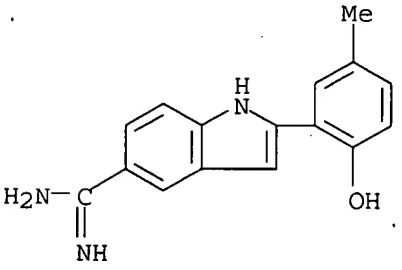
RN 277312-41-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-methyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



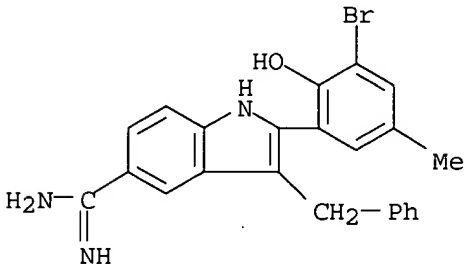
RN 277312-48-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-3,5-dimethylphenyl)- (9CI) (CA INDEX NAME)



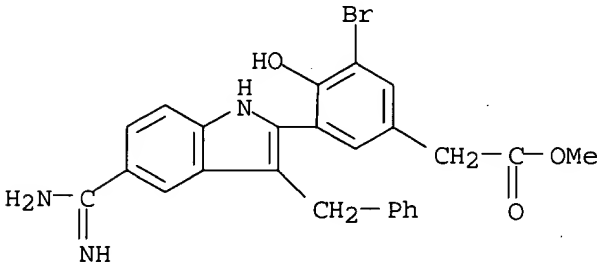
RN 277312-51-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



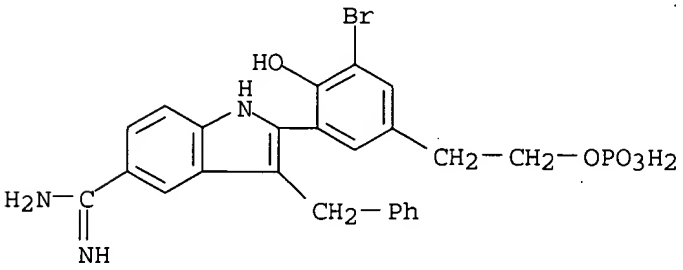
RN 277312-53-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



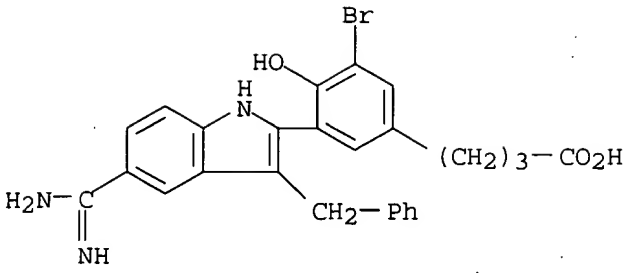
RN 277312-74-0 CAPLUS
CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



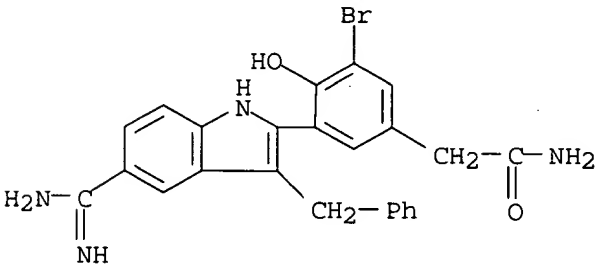
RN 277312-82-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[3-bromo-2-hydroxy-5-[2-(phosphonooxy)ethyl]phenyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



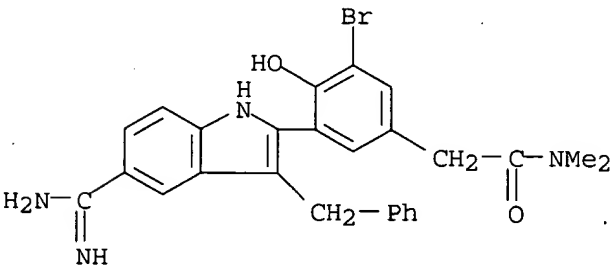
RN 277312-84-2 CAPLUS
CN Benzenebutanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



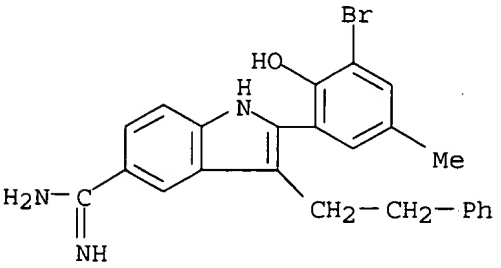
RN 277312-85-3 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



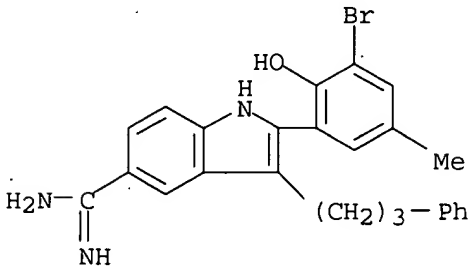
RN 277312-86-4 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-N,N-dimethyl- (9CI) (CA INDEX NAME)



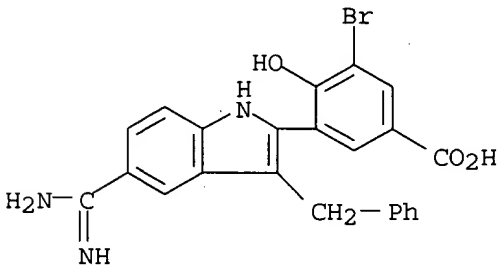
RN 368878-92-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-(2-phenylethyl)- (9CI) (CA INDEX NAME)



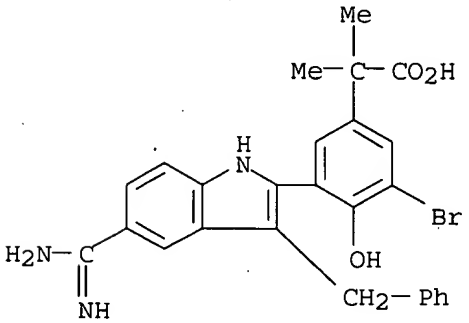
RN 368878-93-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



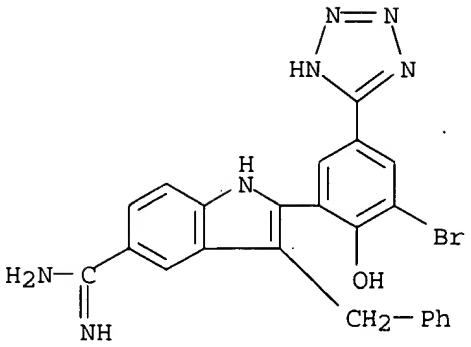
RN 368878-94-8 CAPLUS
CN Benzoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



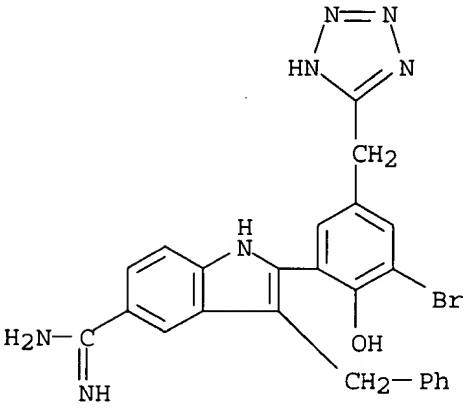
RN 368878-95-9 CAPLUS
CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-.alpha.,.alpha.-dimethyl- (9CI) (CA INDEX NAME)



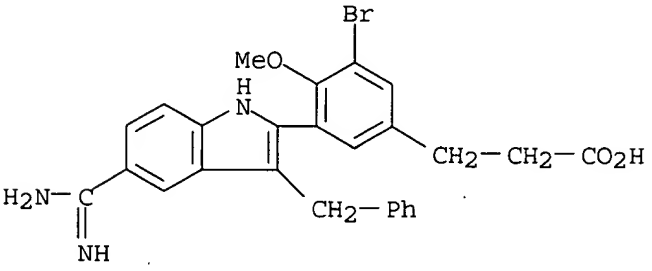
RN 368878-96-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[3-bromo-2-hydroxy-5-(1H-tetrazol-5-yl)phenyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



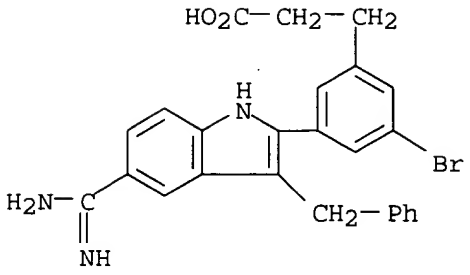
RN 368878-97-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[3-bromo-2-hydroxy-5-(1H-tetrazol-5-ylmethyl)phenyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 368878-98-2 CAPLUS
CN Benzenepropanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-methoxy- (9CI) (CA INDEX NAME)



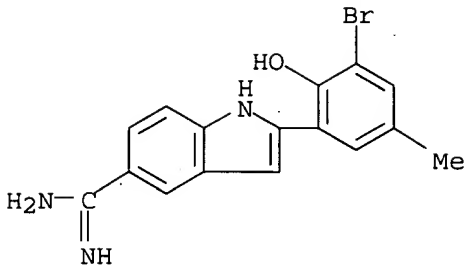
RN 368878-99-3 CAPLUS
CN Benzenepropanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo- (9CI) (CA INDEX NAME)



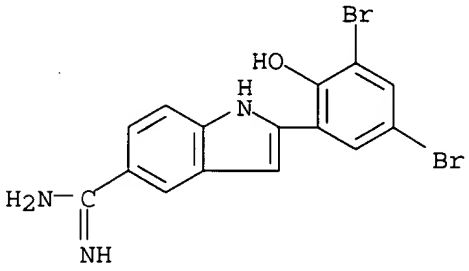
AB The development of potent and selective small mol. inhibitors of factor Xa is described. Inhibition of thrombin and crystal structure of several of the compds. complexed with thrombin is also described. The compds. showed anticoagulant activity. The synthesis of the phenylindolecarboxamide compds. is illustrated.

RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

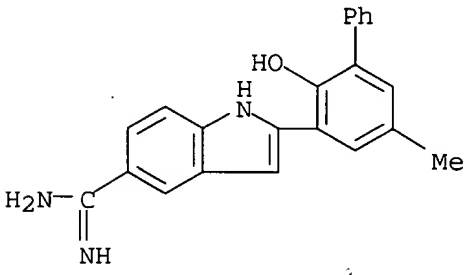
L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:500142 CAPLUS
DN 135:235905
TI Development of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode: Inhibitors of urokinase-type plasminogen activator and factor Xa
AU Verner, Erik; Katz, Bradley A.; Spencer, Jeffrey R.; Allen, Darin; Hataye, Jason; Hruzewicz, Witold; Hui, Hon C.; Kolesnikov, Aleksandr; Li, Yong; Luong, Christine; Martelli, Arnold; Radika, Kesavan; Rai, Roopa; She, Miles; Shrader, William; Sprengeler, Paul A.; Trapp, Sean; Wang, Jing; Young, Wendy B.; Mackman, Richard L.
CS Departments of Medicinal Chemistry Structural Biology and Biochemistry and Enzymology, Axys Pharmaceuticals Inc., South San Francisco, CA, 94080, USA
SO Journal of Medicinal Chemistry (2001), 44(17), 2753-2771
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
IT **277312-31-9P 277312-40-0P 277312-41-1P**
277312-42-2P 277312-44-4P 360791-79-3P
360791-81-7P 360791-83-9P 360791-85-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and biol. activity of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode and inhibitors of urokinase-type plasminogen activator and factor Xa)
RN 277312-31-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



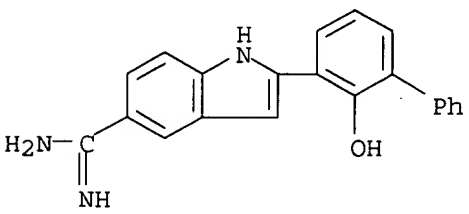
RN 277312-40-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dibromo-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 277312-41-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-methyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)

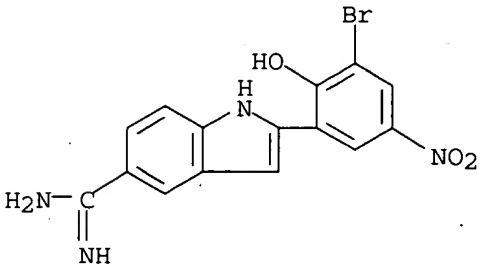


RN 277312-42-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)

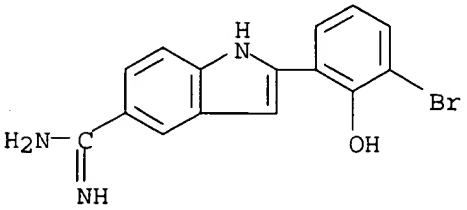


RN 277312-44-4 CAPLUS

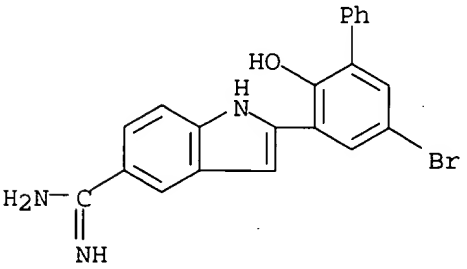
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-nitrophenyl)- (9CI) (CA INDEX NAME)



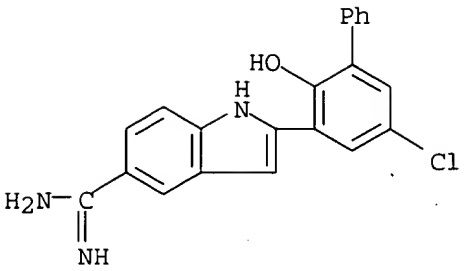
RN 360791-79-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



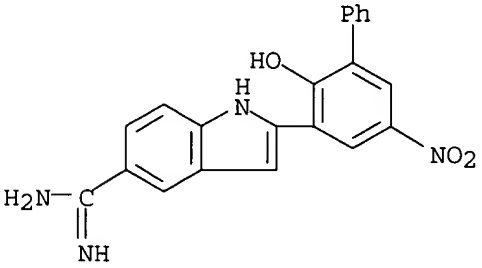
RN 360791-81-7 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(5-bromo-2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



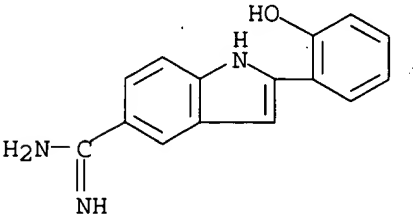
RN 360791-83-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(5-chloro-2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



RN 360791-85-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-nitro[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)



IT **179748-10-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biol. activity of serine protease inhibitors displaying a multicentered short (<2.3 .ANG.) hydrogen bond binding mode and inhibitors of urokinase-type plasminogen activator and factor Xa)
RN 179748-10-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)

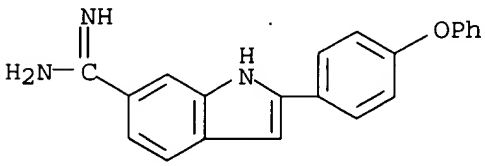


AB Novel scaffolds that bind to serine proteases through a unique network of short hydrogen bonds to the catalytic Ser195 have been developed. The resulting potent serine protease inhibitors were designed from lead mol. 2-(2-hydroxyphenyl)1H-benzoimidazole-5-carboxamidine, 6b, which is known to display several modes of binding. For instance, 6b can recruit zinc and bind in a manner similar to that reported by bis(5-amidino-2-benzimidazolyl)methane (BABIM) (Nature 1998, 391, 608-612). Alternatively, 6b can bind in the absence of zinc through a multicentered network of short (<2.3 .ANG.) hydrogen bonds. The lead structure was optimized in the zinc-independent binding mode toward a panel of six human serine proteases to yield optimized inhibitors such as 2-(3-bromo-2-hydroxy-5-methylphenyl)-1H-indole-5-carboxamidine, 22a, and

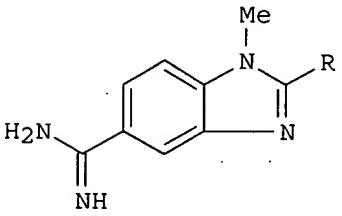
2-(2-hydroxybiphenyl-3-yl)-1H-indole-5-carboxamidine, 22f. Structure-activity relationships detd. that, apart from the amidine function, an indole or benzimidazole and an ortho substituted phenol group were also essential components for optimal potency. The affinities (Ki) of 22a and 22f, for example, bearing these groups ranged from 8 to 600 nM toward a panel of six human serine proteases. High-resoln. crystal structures revealed that the binding mode of these mols. in several of the enzymes was identical to that of 6b and involved short (<2.3 .ANG.) hydrogen bonds among the inhibitor hydroxyl oxygen, Ser195, and a water mol. trapped in the oxyanion hole. In summation, novel and potent trypsin-like serine protease inhibitors possessing a unique mode of binding have been discovered.

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:456650 CAPLUS
DN 135:195528
TI Amidino benzimidazole inhibitors of bacterial two-component systems
AU Weidner-Wells, M. A.; Ohemeng, K. A.; Nguyen, V. N.; Fraga-Spano, S.; Macielag, M. J.; Werblood, H. M.; Foleno, B. D.; Webb, G. C.; Barrett, J. F.; Hlasta, D. J.
CS Drug Discovery, The R. W. Johnson Pharmaceutical Research Institute, Raritan, NJ, 08869, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(12), 1545-1548
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 135:195528
IT **357156-54-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. and antibacterial activity of amidino benzimidazole and benzoxazole inhibitors of bacterial two-component systems)
RN 357156-54-8 CAPLUS
CN 1H-Indole-6-carboximidamide, 2-(4-phenoxyphenyl)- (9CI) (CA INDEX NAME)



GI



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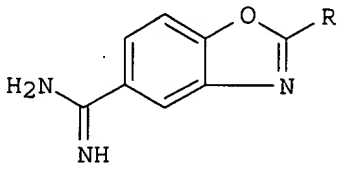

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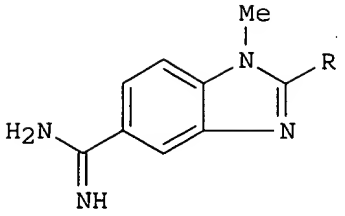

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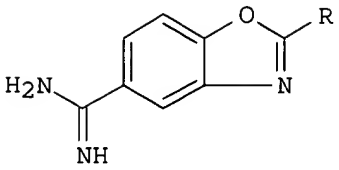
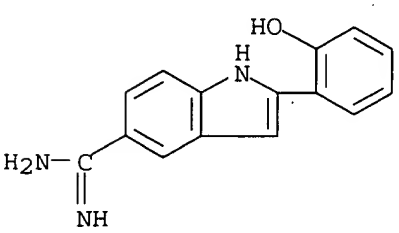


II

AB Amidino benzimidazoles, such as I (R = C6H4-4-OPh), were identified as inhibitors of the bacterial KinA/Spo0F two-component system (TCS). Many of these inhibitors exhibit good in vitro antibacterial activity against a variety of susceptible and resistant Gram-pos. organisms. The moiety at the 2-position of the benzimidazole was extensively modified. In addn., the regioisomeric benzoxazoles II [R = C6H4-4-OPh, C6H2-2-OH-3,5-(CMe3)2], heterocyclic replacements for the benzimidazole, were synthesized and their activity against the TCS evaluated.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:246441 CAPLUS
DN 135:89065
TI A Novel Serine Protease Inhibition Motif Involving a Multi-centered Short Hydrogen Bonding Network at the Active Site
AU Katz, Bradley A.; Elrod, Kyle; Luong, Christine; Rice, Mark J.; Mackman, Richard L.; Sprengeler, Paul A.; Spencer, Jeffrey; Hataye, Jason; Janc, James; Link, John; Litvak, Joane; Rai, Roopa; Rice, Ken; Sideris, Steve; Verner, Erik; Young, Wendy
CS Axys Pharmaceuticals Corporation, South San Francisco, CA, 94080, USA
SO Journal of Molecular Biology (2001), 307(5), 1451-1486
CODEN: JMOBAK; ISSN: 0022-2836
PB Academic Press
DT Journal
LA English
IT **179748-10-8**, APC 8328
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(novel serine protease inhibition motif involving a multi-centered short hydrogen bonding network at active site)
RN 179748-10-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



AB We describe a new serine protease inhibition motif in which binding is mediated by a cluster of very short hydrogen bonds (<2.3 .ANG.) at the

active site. This protease-inhibitor binding paradigm is obsd. at high resoln. in a large set of crystal structures of trypsin, thrombin, and urokinase-type plasminogen activator (uPA) bound with a series of small mol. inhibitors (2-(2-phenol)indoles and 2-(2-phenol)benzimidazoles). In each complex there are eight enzyme-inhibitor or enzyme-water-inhibitor hydrogen bonds at the active site, three of which are very short. These short hydrogen bonds connect a triangle of oxygen atoms comprising O.gamma.Ser195, a water mol. co-bound in the oxyanion hole (H2Ooxy), and the phenolate oxygen atom of the inhibitor (O6'). Two of the other hydrogen bonds between the inhibitor and active site of the trypsin and uPA complexes become short in the thrombin counterparts, extending the three-centered short hydrogen-bonding array into a tetrahedral array of atoms (three oxygen and one nitrogen) involved in short hydrogen bonds. In the uPA complexes, the extensive hydrogen-bonding interactions at the active site prevent the inhibitor S1 amidine from forming direct hydrogen bonds with Asp189 because the S1 site is deeper in uPA than in trypsin or thrombin. Ionization equil. at the active site assocd. with inhibitor binding are probed through detn. and comparison of structures over a wide range of pH (3.5 to 11.4) of thrombin complexes and of trypsin complexes in three different crystal forms. The high-pH trypsin-inhibitor structures suggest that His57 is protonated at pH values as high as 9.5. The pH-dependent inhibition of trypsin, thrombin, uPA and factor Xa by 2-(2-phenol)benzimidazole analogs in which the pKa of the phenol group is modulated is shown to be consistent with a binding process involving ionization of both the inhibitor and the enzyme. These data further suggest that the pKa of His57 of each protease in the unbound state in soln. is about the same, .apprx.6.8. By comparing inhibition consts. (Ki values), inhibitor solubilities, inhibitor conformational energies and corresponding structures of short and normal hydrogen bond-mediated complexes, we have estd. the contribution of the short hydrogen bond networks to inhibitor affinity (.apprx.1.7 kcal/mol). The structures and Ki values assocd. with the short hydrogen-bonding motif are compared with those corresponding to an alternate, Zn2+-mediated inhibition motif at the active site. Structural differences among apo-enzymes, enzyme-inhibitor and enzyme-inhibitor-Zn2+ complexes are discussed in the context of affinity determinants, selectivity development, and structure-based inhibitor design. (c) 2001 Academic Press.

RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2001:178434 CAPLUS
DN 134:222629
TI Preparation of indoles as antagonists of gonadotropin releasing hormone
IN Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Lin, Peter; Ponpipom, Mitree M.; Wyvratt, Matthew J.; Girotra, Narindar N.; Young, Jonathan
PA Merck & Co., Inc., USA
SO U.S., 53 pp., Cont.-in-part of U.S. 5,780,437.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6200957	B1	20010313	US 1998-115497	19980714
				US 1995-8633P P	19951214
				US 1996-760816 A2	19961205

US 5780437	A	19980714	US 1996-760816	19961205
JP 2001106685	A2	20010417	JP 2000-257791	19961210
			US 1995-8633P P	19951214
			GB 1996-3242 A	19960216
			JP 1997-522124 A3	19961210
ZA 9610536	A	19970814	ZA 1996-10536	19961213
			US 1995-8633P P	19951214
CA 2337407	AA	20000127	CA 1999-2337407	19990709
			US 1998-115497 A	19980714
			WO 1999-US15581W	19990709
WO 2000004013	A1	20000127	WO 1999-US15581	19990709
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
			US 1998-115497 A	19980714
AU 9949816	A1	20000207	AU 1999-49816	19990709
			US 1998-115497 A	19980714
			WO 1999-US15581W	19990709
EP 1095038	A1	20010502	EP 1999-933850	19990709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
			US 1998-115497 A	19980714
			WO 1999-US15581W	19990709
JP 2002520409	T2	20020709	JP 2000-560119	19990709
			US 1998-115497 A	19980714
			WO 1999-US15581W	19990709

PATENT FAMILY INFORMATION:

FAN 1997:511777

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9721704	A1	19970619	WO 1996-US19444	19961210
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	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
	CA 2240108	AA	19970619	CA 1996-2240108	19961210
				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
	AU 9714106	A1	19970703	AU 1997-14106	19961210
	AU 707641	B2	19990715		
				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
				WO 1996-US19444W	19961210
	EP 873336	A1	19981028	EP 1996-944249	19961210
	EP 873336	B1	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
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	CN 1208412	A	19990217	CN 1996-199872 19961210
				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
	JP 11506471	T2	19990608	JP 1996-522124 19961210
				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
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	JP 3230818	B2	20011119	JP 1997-522124 19961210
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				GB 1996-3242 A 19960216
	AT 215081	E	20020415	AT 1996-944249 19961210
				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
				WO 1996-US19444W 19961210
	ES 2174129	T3	20021101	ES 1996-944249 19961210
				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
	ZA 9610536	A	19970814	ZA 1996-10536 19961213
				US 1995-8633P P 19951214
	NO 9802729	A	19980813	NO 1998-2729 19980612
				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
				WO 1996-US19444W 19961210

FAN 1998:479019

	PATENT NO.	KIND	DATE	APPLICATION NO. DATE
PI	US 5780437	A	19980714	US 1996-760816 19961205
	US 6200957	B1	20010313	US 1998-115497 19980714
				US 1995-8633P P 19951214
				US 1996-760816 A2 19961205

FAN 2000:68450

	PATENT NO.	KIND	DATE	APPLICATION NO. DATE
PI	WO 2000004013	A1	20000127	WO 1999-US15581 19990709
	W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
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				US 1998-115497 A 19980714
	US 6200957	B1	20010313	US 1998-115497 19980714
				US 1995-8633P P 19951214
				US 1996-760816 A2 19961205
	CA 2337407	AA	20000127	CA 1999-2337407 19990709
				US 1998-115497 A 19980714
				WO 1999-US15581W 19990709
	AU 9949816	A1	20000207	AU 1999-49816 19990709
				US 1998-115497 A 19980714
				WO 1999-US15581W 19990709
	EP 1095038	A1	20010502	EP 1999-933850 19990709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

US 1998-115497 A 19980714
WO 1999-US15581W 19990709

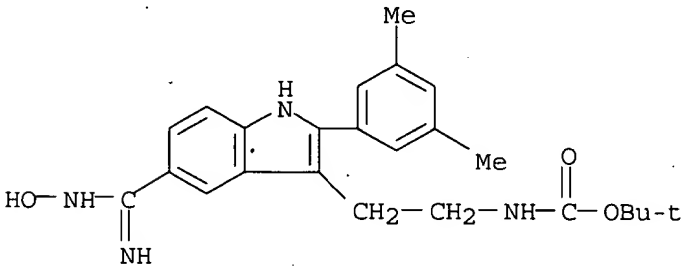
JP 2002520409 T2 20020709 JP 2000-560119 19990709
US 1998-115497 A 19980714
WO 1999-US15581W 19990709

OS MARPAT 134:222629

IT **192644-10-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of indoles as antagonists of gonadotropin.releasing hormone)

RN 192644-10-3 CAPLUS

CN Carbamic acid, [2-[2-(3,5-dimethylphenyl)-5-[(hydroxyamino)iminomethyl]-1H-indol-3-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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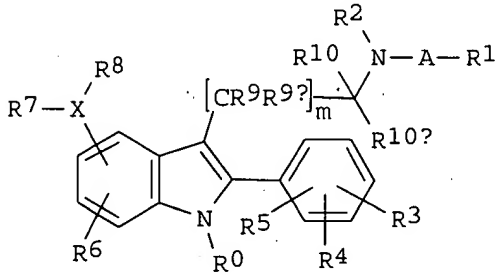

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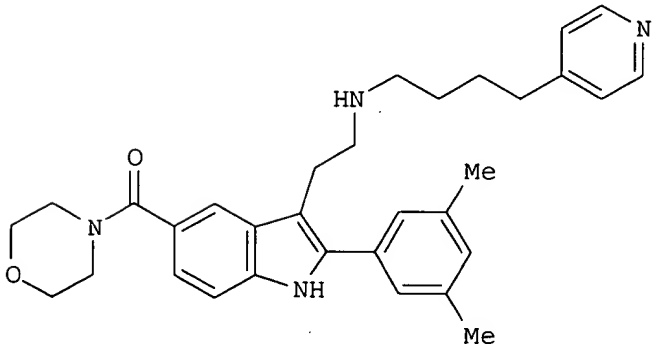

II

AB The title compds. [I; A = alkyl, cycloalkyl, alkenyl, etc.; R0 = H, alkyl, aryl, etc.; R1 = (un)substituted 3-pyridyl, 4-pyridyl, benzimidazolyl, etc.; R2 = H, alkyl, aryl, etc.; R2 and A taken together form 5-7 membered ring; R3-R5 = H, alkyl, alkenyl, etc.; R3 and R4 taken together form 3-7 membered carbocyclic ring or heterocyclic ring contg. 1-3 heteroatoms selected from, N, O, S; R6 = H, alkyl, aryl, etc.; R7 = H, alkyl (when X = H, halo, then R7 is absent); R8 = heterocyclic ring, bicyclic heterocyclic ring, etc.; R7 and R8 taken together form (un)substituted heterocyclic ring contg. one or more heteroatoms selected form N, O or S; X = N, O, CO, etc.; m = 0-3; R9, R9a = H, alkyl, aryl, etc.; R10, R10a = H, alkyl, aryl, etc.], useful as antagonists of GnRH and as such may be useful for the treatment of a variety of sex-hormone related and other conditions in both men and women, were prepd. E.g., a multi-step synthesis of the indole II was given. Compds. I are effective at 0.001-1 mg/kg/day.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2000:421114 CAPLUS
DN 133:58803
TI Preparation of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors
IN Allen, Darin Arthur; Hataye, Jason M.; Hruzewicz, Witold N.; Kolesnikov, Aleksandr; Mackman, Richard Laurence; Rai, Roopa; Spencer, Jeffrey R.; Verner, Erik J.; Young, Wendy B.
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000035886	A2	20000622	WO 1999-US30302	19991217
	WO 2000035886	A3	20001026		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1998-113007PP	19981218
	EP 1140859	A2	20011010	EP 1999-968917	19991217
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				US 1998-113007PP	19981218
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	BR 9916363	A	20011211	BR 1999-16363	19991217
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				WO 1999-US30302W	19991217
	EE 200100323	A	20020815	EE 2001-20010032319991217	
				US 1998-113007PP	19981218
				WO 1999-US30302W	19991217
	JP 2002532479	T2	20021002	JP 2000-588148	19991217

US 1998-113007PP 19981218
WO 1999-US30302W 19991217

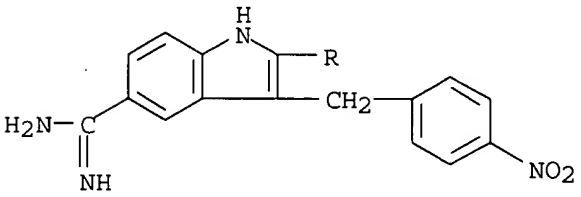
NO 2001002980 A 20010801 NO 2001-2980 20010615
US 1998-113007PP 19981218
WO 1999-US30302W 19991217

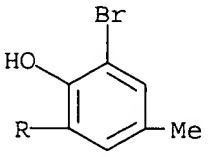
OS MARPAT 133:58803

IT **277312-56-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors)

RN 277312-56-8 CAPLUS

CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)





IT **277312-20-6P 277312-21-7P 277312-22-8P**
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277312-29-5P 277312-30-8P 277312-31-9P
277312-32-0P 277312-33-1P 277312-34-2P
277312-35-3P 277312-36-4P 277312-37-5P
277312-38-6P 277312-39-7P 277312-40-0P
277312-41-1P 277312-42-2P 277312-43-3P
277312-44-4P 277312-45-5P 277312-46-6P
277312-47-7P 277312-48-8P 277312-49-9P
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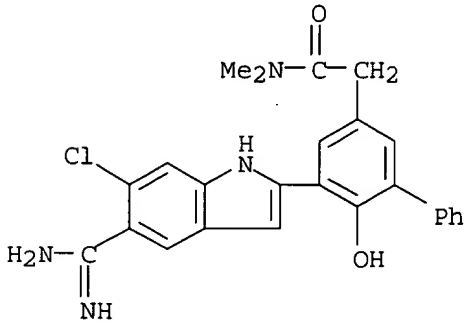
277312-53-5P 277312-54-6P 277312-57-9P
277312-59-1P 277312-60-4P 277312-61-5P
277312-62-6P 277312-74-0P 277312-75-1P
277312-76-2P 277312-77-3P 277312-78-4P
277312-79-5P 277312-80-8P 277312-81-9P
277312-82-0P 277312-83-1P 277312-84-2P
277312-85-3P 277312-86-4P 277312-87-5P
277312-88-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-arylindole- or -benzimidazolecarboxamidines and analogs as

serine protease inhibitors)

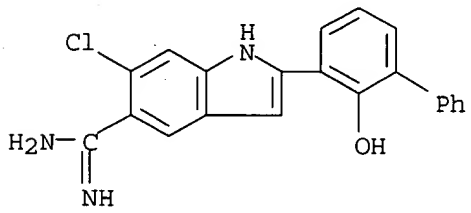
RN 277312-20-6 CAPLUS

CN [1,1'-Biphenyl]-3-acetamide, 5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy-N,N-dimethyl- (9CI) (CA INDEX NAME)



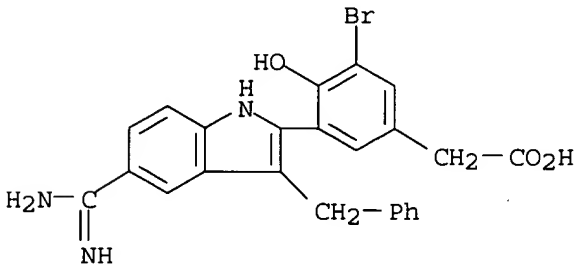
RN 277312-21-7 CAPLUS

CN 1H-Indole-5-carboximidamide, 6-chloro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



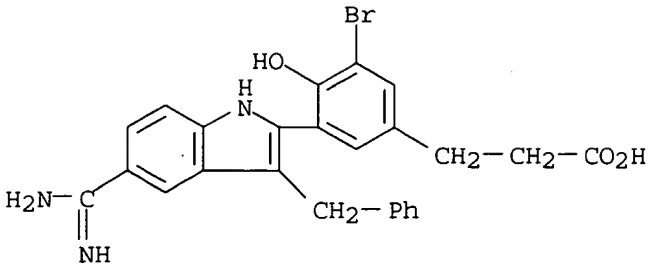
RN 277312-22-8 CAPLUS

CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)

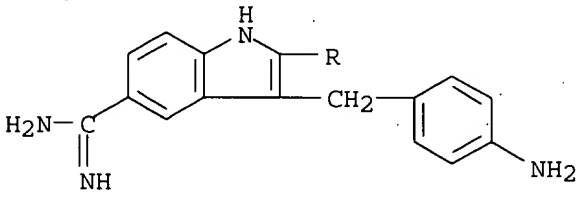


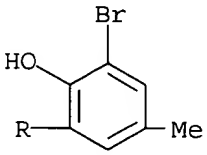
RN 277312-23-9 CAPLUS

CN Benzenepropanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)

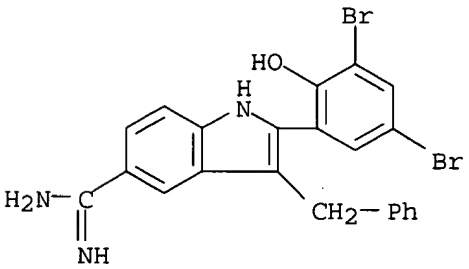


RN 277312-24-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 3-[(4-aminophenyl)methyl]-2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)

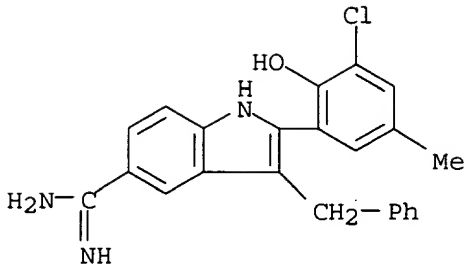




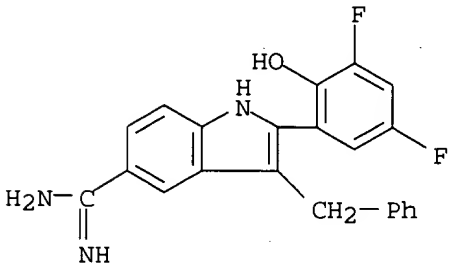
RN 277312-25-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dibromo-2-hydroxyphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



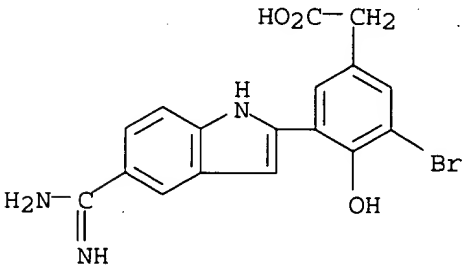
RN 277312-26-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-chloro-2-hydroxy-5-methylphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



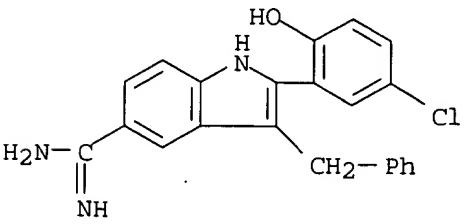
RN 277312-27-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-difluoro-2-hydroxyphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



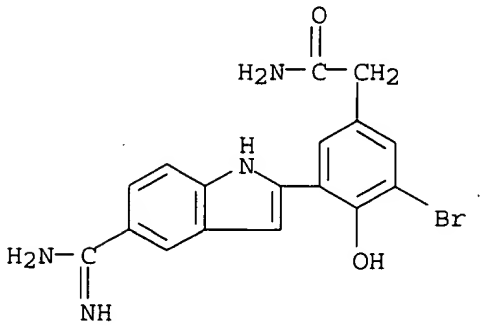
RN 277312-28-4 CAPLUS
CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



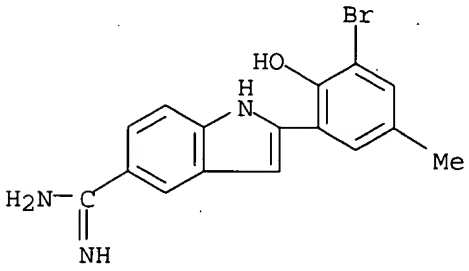
RN 277312-29-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(5-chloro-2-hydroxyphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



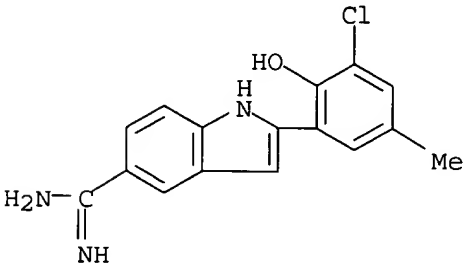
RN 277312-30-8 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



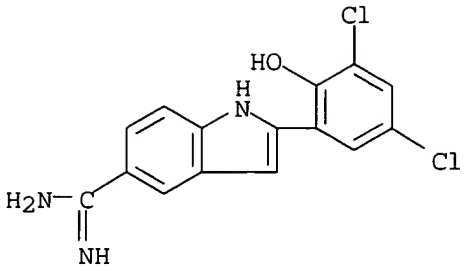
RN 277312-31-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



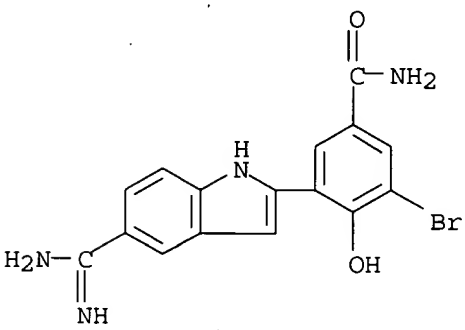
RN 277312-32-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-chloro-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



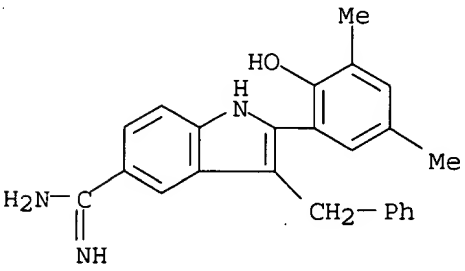
RN 277312-33-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dichloro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



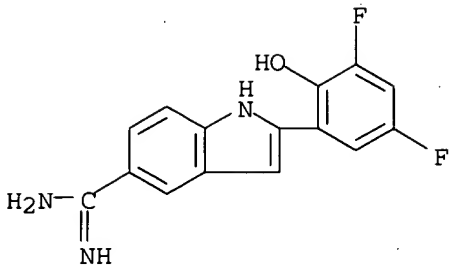
RN 277312-34-2 CAPLUS
CN Benzamide, 3-[5-(aminoiminomethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



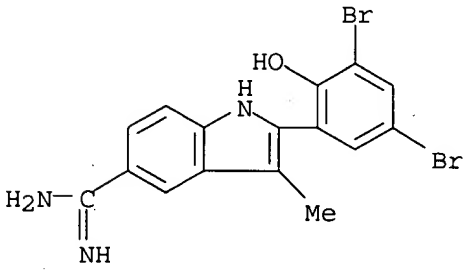
RN 277312-35-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-3,5-dimethylphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



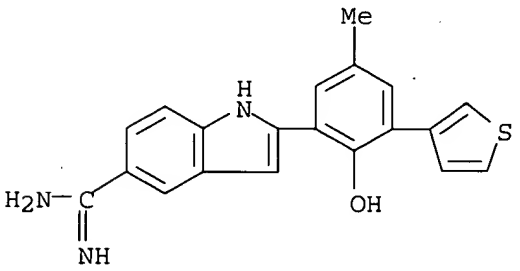
RN 277312-36-4 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-difluoro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



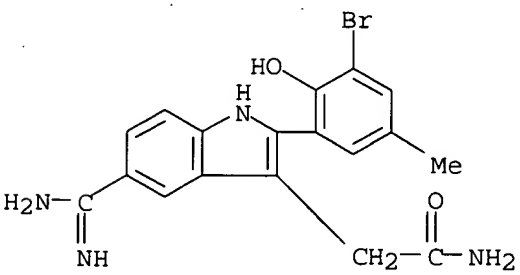
RN 277312-37-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dibromo-2-hydroxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)



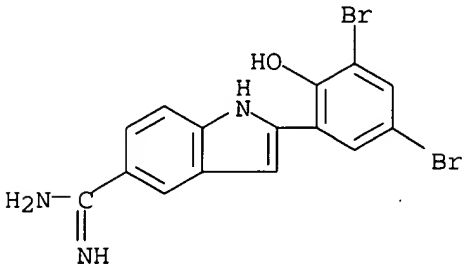
RN 277312-38-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[2-hydroxy-5-methyl-3-(3-thienyl)phenyl]- (9CI) (CA INDEX NAME)



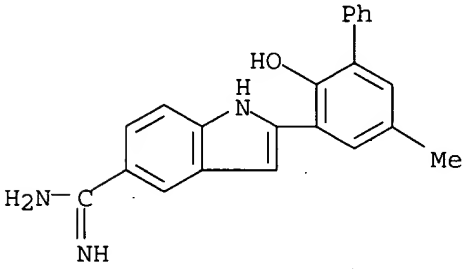
RN 277312-39-7 CAPLUS
CN 1H-Indole-3-acetamide, 5-(aminoiminomethyl)-2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



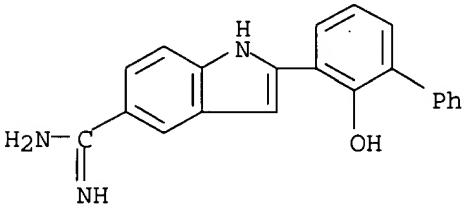
RN 277312-40-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3,5-dibromo-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



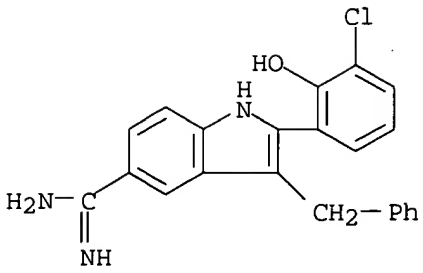
RN 277312-41-1 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-methyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



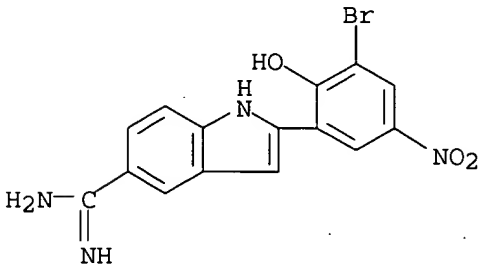
RN 277312-42-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



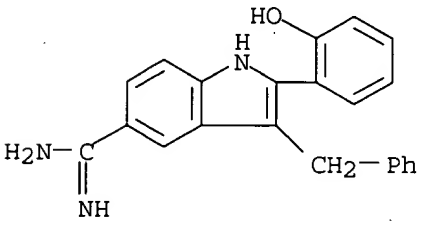
RN 277312-43-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-chloro-2-hydroxyphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



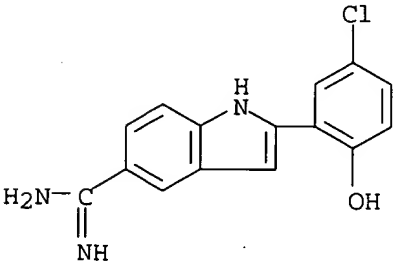
RN 277312-44-4 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-nitrophenyl)- (9CI) (CA INDEX NAME)



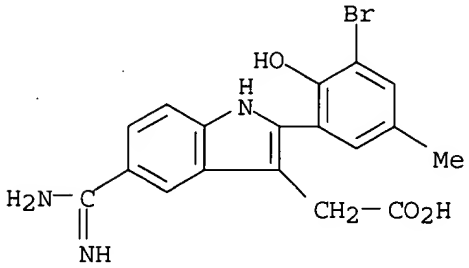
RN 277312-45-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxyphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



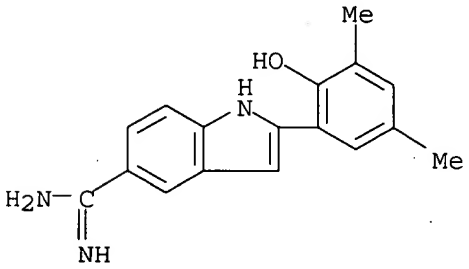
RN 277312-46-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(5-chloro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



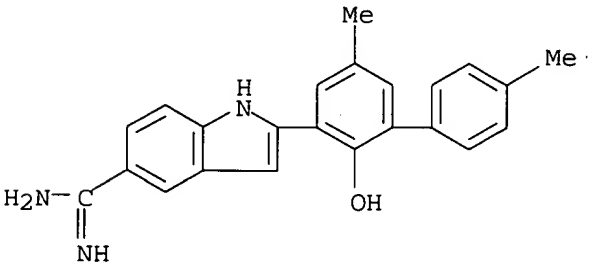
RN 277312-47-7 CAPLUS
CN 1H-Indole-3-acetic acid, 5-(aminoiminomethyl)-2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



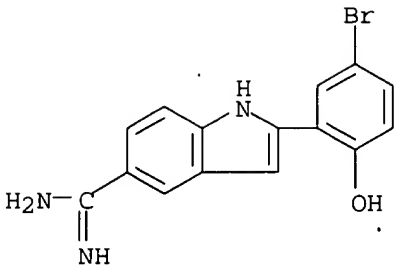
RN 277312-48-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-3,5-dimethylphenyl)- (9CI) (CA INDEX NAME)



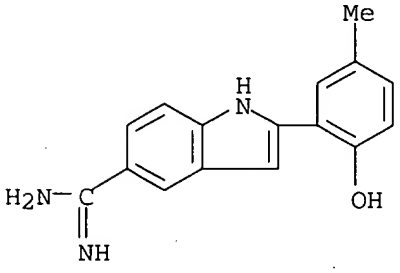
RN 277312-49-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-4',5-dimethyl[1,1'-biphenyl]-3-yl)- (9CI) (CA INDEX NAME)



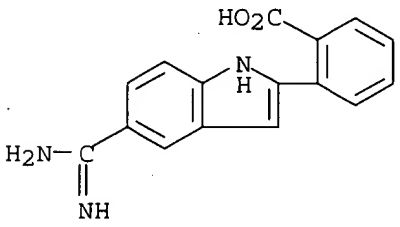
RN 277312-50-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(5-bromo-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



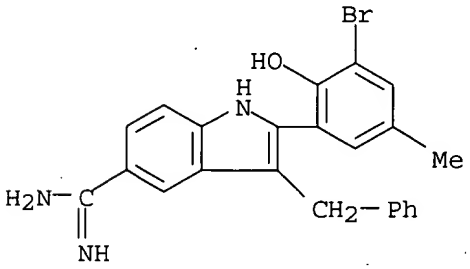
RN 277312-51-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



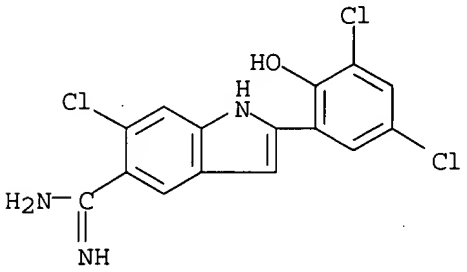
RN 277312-52-4 CAPLUS
CN Benzoic acid, 2-[5-(aminoiminomethyl)-1H-indol-2-yl]- (9CI) (CA INDEX NAME)



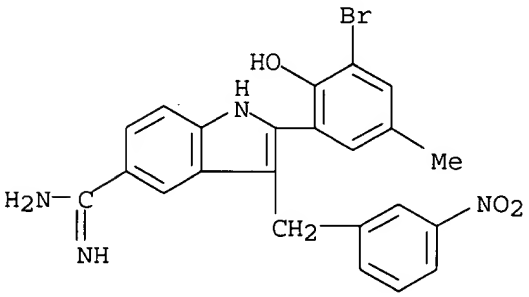
RN 277312-53-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



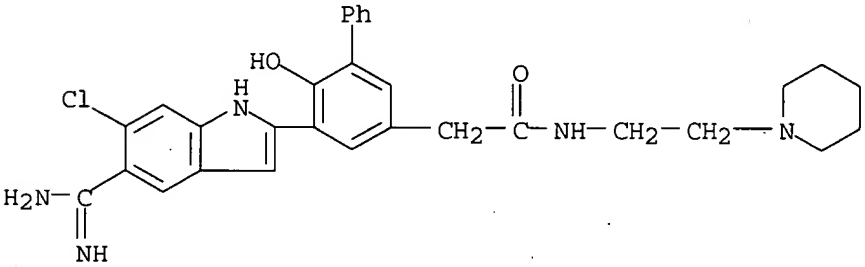
RN 277312-54-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-(3,5-dichloro-2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



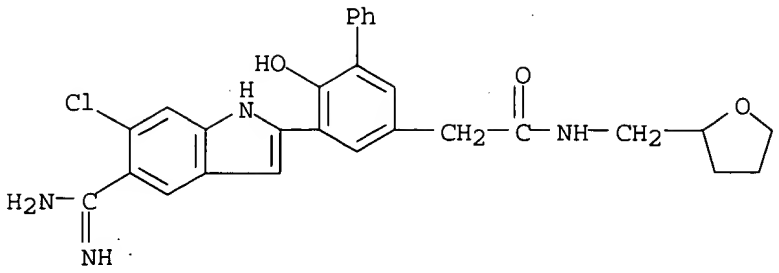
RN 277312-57-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(3-bromo-2-hydroxy-5-methylphenyl)-3-[(3-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)



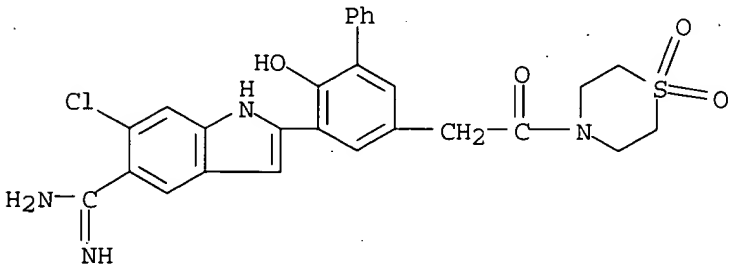
RN 277312-59-1 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy-N-[2-(1-piperidinyl)ethyl]- (9CI) (CA INDEX NAME)



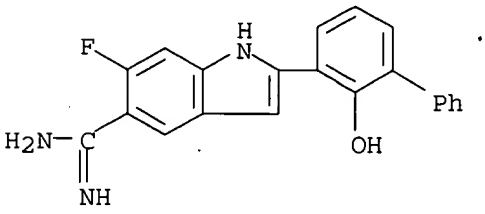
RN 277312-60-4 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy-N-[(tetrahydro-2-furanyl)methyl]- (9CI) (CA INDEX NAME)



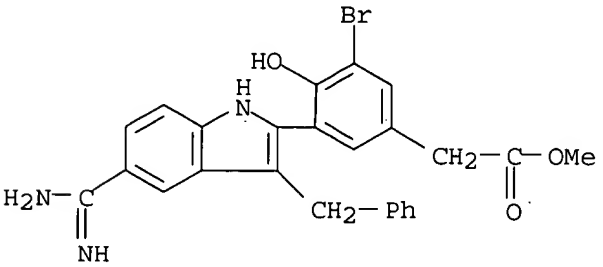
RN 277312-61-5 CAPLUS
CN Thiomorpholine, 4-[[5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]acetyl]-, 1,1-dioxide (9CI) (CA INDEX NAME)



RN 277312-62-6 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-fluoro-2-(2-hydroxy[1,1'-biphenyl]-3-yl)-(9CI) (CA INDEX NAME)

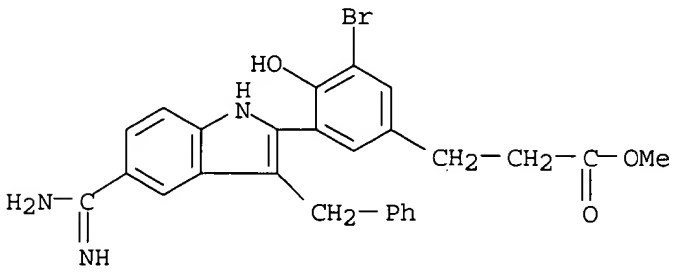


RN 277312-74-0 CAPLUS
CN Benzeneacetic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

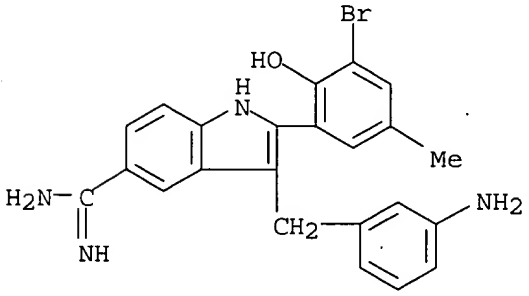


RN 277312-75-1 CAPLUS

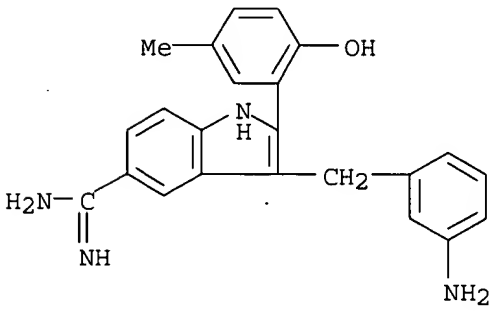
CN Benzenepropanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



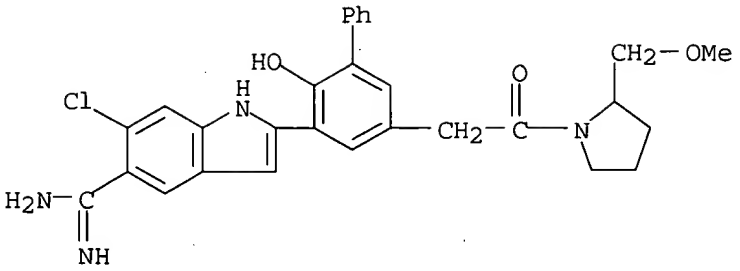
RN 277312-76-2 CAPLUS
CN 1H-Indole-5-carboximidamide, 3-[(3-aminophenyl)methyl]-2-(3-bromo-2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



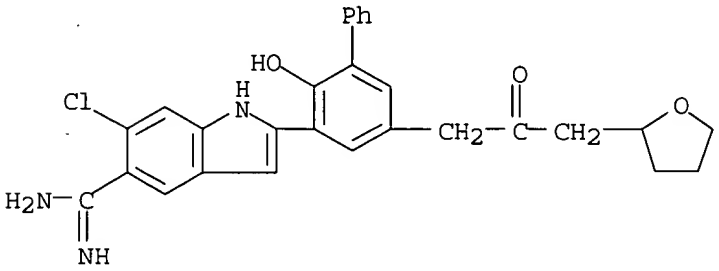
RN 277312-77-3 CAPLUS
CN 1H-Indole-5-carboximidamide, 3-[(3-aminophenyl)methyl]-2-(2-hydroxy-5-methylphenyl)- (9CI) (CA INDEX NAME)



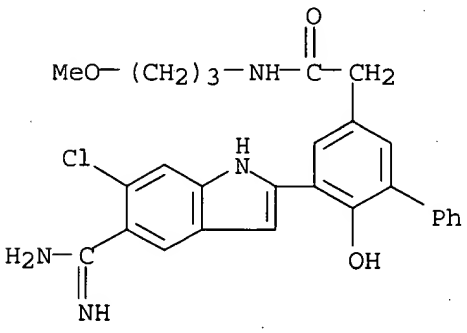
RN 277312-78-4 CAPLUS
CN Pyrrolidine, 1-[[5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]acetyl]-2-(methoxymethyl)- (9CI) (CA INDEX NAME)



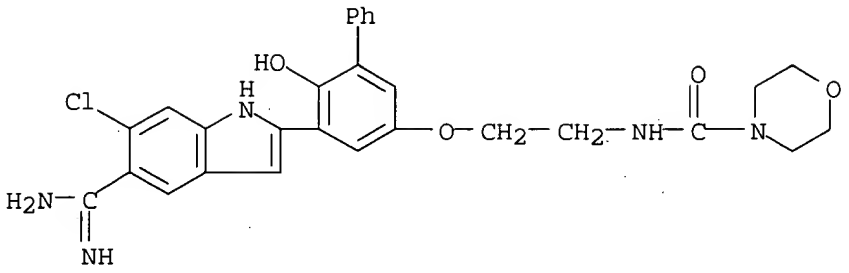
RN 277312-79-5 CAPLUS
CN 1H-Indole-5-carboximidamide, 6-chloro-2-[2-hydroxy-5-[2-oxo-3-(tetrahydro-2-furanyl)propyl][1,1'-biphenyl]-3-yl]- (9CI) (CA INDEX NAME)



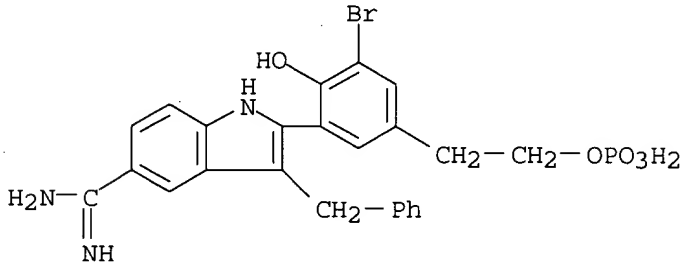
RN 277312-80-8 CAPLUS
CN [1,1'-Biphenyl]-3-acetamide, 5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy-N-(3-methoxypropyl)- (9CI) (CA INDEX NAME)



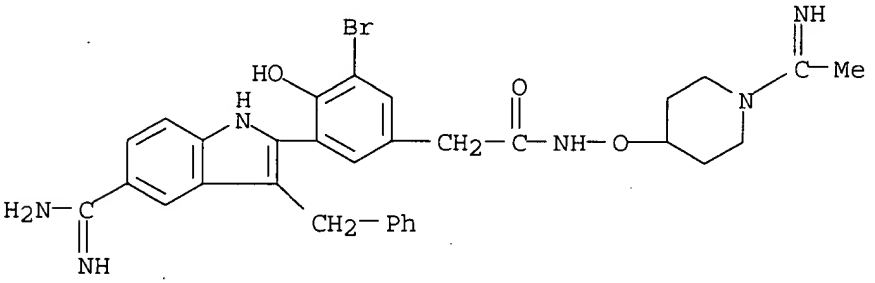
RN 277312-81-9 CAPLUS
CN 4-Morpholinecarboxamide, N-[2-[[5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy[1,1'-biphenyl]-3-yl]oxy]ethyl]- (9CI) (CA INDEX NAME)



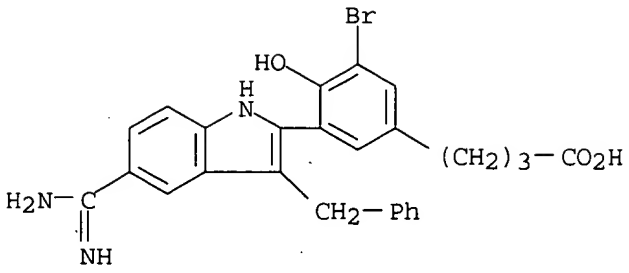
RN 277312-82-0 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-[3-bromo-2-hydroxy-5-[2-(phosphonooxy)ethyl]phenyl]-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



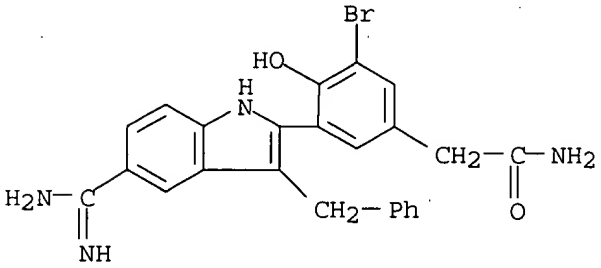
RN 277312-83-1 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-N-[[1-(1-iminoethyl)-4-piperidinyl]oxy]- (9CI) (CA INDEX NAME)



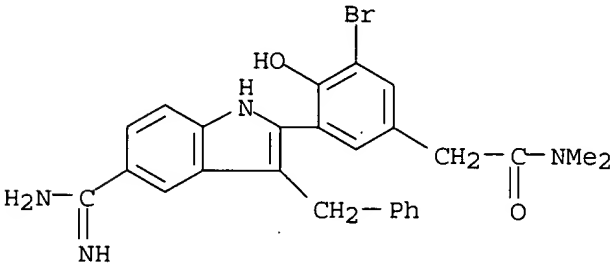
RN 277312-84-2 CAPLUS
CN Benzenebutanoic acid, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



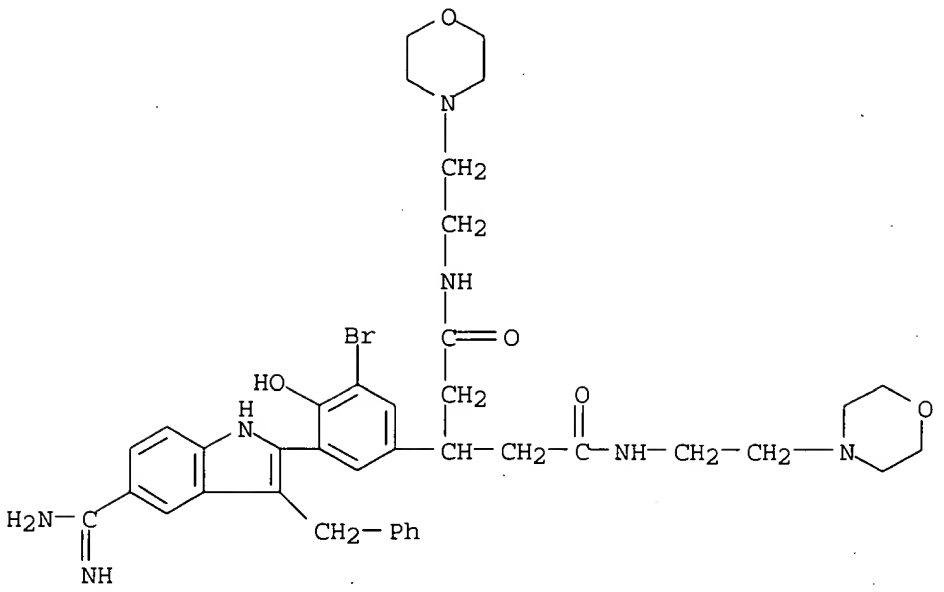
RN 277312-85-3 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



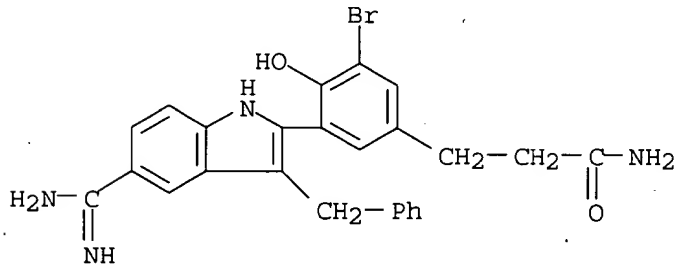
RN 277312-86-4 CAPLUS
CN Benzeneacetamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 277312-87-5 CAPLUS
CN Pentanediamide, 3-[3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxyphenyl]-N,N'-bis[2-(4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 277312-88-6 CAPLUS
CN Benzenepropanamide, 3-[5-(aminoiminomethyl)-3-(phenylmethyl)-1H-indol-2-yl]-5-bromo-4-hydroxy- (9CI) (CA INDEX NAME)



IT **277313-28-7P 277313-29-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2-arylindole- or -benzimidazolecarboxamidines and analogs as serine protease inhibitors)
RN 277313-28-7 CAPLUS
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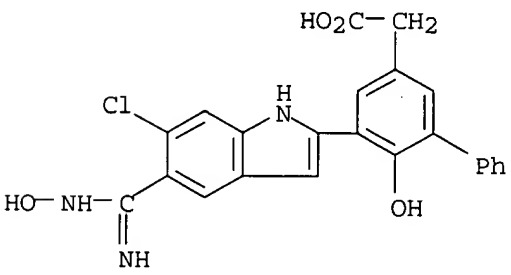
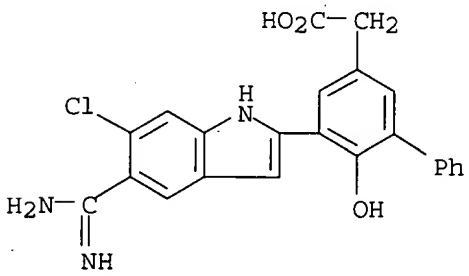


RN 277313-29-8 CAPLUS
CN [1,1'-Biphenyl]-3-acetic acid, 5-[5-(aminoiminomethyl)-6-chloro-1H-indol-2-yl]-6-hydroxy- (9CI) (CA INDEX NAME)



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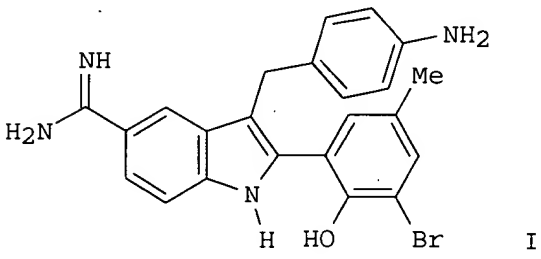

I

AB R1Z1Z2R2 [I; R1 = H2NC(:NH), etc.; R2 = halo, OH, CO2H, phenyl(alkyl)oxy, etc.; Z1 = (un)substituted indolylene, -benzimidazolylene, etc.; Z2 = (un)substituted phenylene, pyridinediyl, etc.] were prepd. Thus, 1-(3-bromo-2-hydroxy-5-methylphenyl)-3-(4-nitrophenyl)-1-propanone was condensed with 4-(H2NHN)C6H4C(:NH)NH2 and the product cyclized to give, after redn., title compd. II. Data for biol. activity of I were given.

L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 2000:68450 CAPLUS
DN 132:107953
TI Preparation of heterocyclic compounds as antagonists of gonadotropin releasing hormone
IN Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Lin, Peter; Ponpipom, Mitree M.; Wyvratt, Matthew J.; Girotra, Narindar N.; Young, Jonathan
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004013	A1	20000127	WO 1999-US15581	19990709

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TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

				US 1998-115497 A 19980714
US 6200957		B1	20010313	US 1998-115497 19980714
				US 1995-8633P P 19951214
				US 1996-760816 A219961205
CA 2337407		AA	20000127	CA 1999-2337407 19990709
				US 1998-115497 A 19980714
				WO 1999-US15581W 19990709
AU 9949816		A1	20000207	AU 1999-49816 19990709
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EP 1095038		A1	20010502	EP 1999-933850 19990709

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				US 1998-115497 A 19980714
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JP 2002520409		T2	20020709	JP 2000-560119 19990709
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PATENT FAMILY INFORMATION:

FAN 1997:511777

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9721704	A1	19970619	WO 1996-US19444	19961210

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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

				US 1995-8633P P 19951214
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CA 2240108		AA	19970619	CA 1996-2240108 19961210
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AU 9714106		A1	19970703	AU 1997-14106 19961210
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				WO 1996-US19444W 19961210
EP 873336		A1	19981028	EP 1996-944249 19961210
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

				US 1995-8633P P 19951214
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				US 1995-8633P P 19951214
				GB 1996-3242 A 19960216
	ZA 9610536	A	19970814	ZA 1996-10536 19961213
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	NO 9802729	A	19980813	NO 1998-2729 19980612
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				GB 1996-3242 A 19960216
				WO 1996-US19444W 19961210

FAN 1998:479019

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5780437	A	19980714	US 1996-760816	19961205
	US 6200957	B1	20010313	US 1998-115497	19980714
				US 1995-8633P P	19951214
				US 1996-760816 A2	19961205

FAN 2001:178434

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6200957	B1	20010313	US 1998-115497	19980714
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				US 1996-760816 A2	19961205
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	WO 2000004013	A1	20000127	WO 1999-US15581	19990709
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	EP 1095038	A1	20010502	EP 1999-933850	19990709
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				US 1998-115497 A	19980714

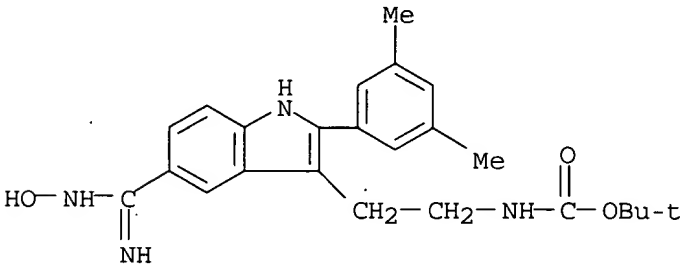
WO 1999-US15581W 19990709
JP 2002520409 T2 20020709 JP 2000-560119 19990709
US 1998-115497 A 19980714
WO 1999-US15581W 19990709

OS MARPAT 132:107953

IT **192644-10-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic compds. as antagonists of gonadotropin releasing hormone)

RN 192644-10-3 CAPLUS

CN Carbamic acid, [2-[2-(3,5-dimethylphenyl)-5-[(hydroxyamino)iminomethyl]-1H-indol-3-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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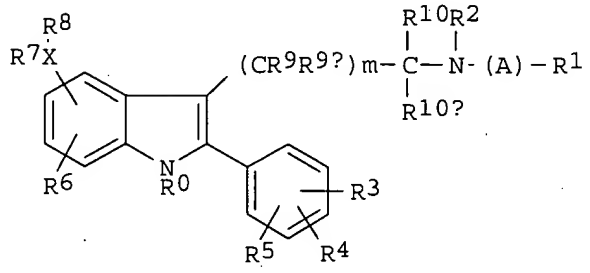

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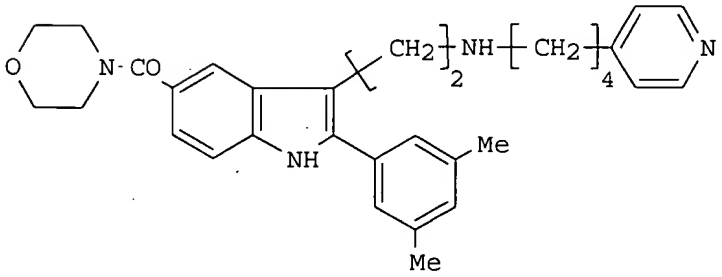

II

AB The title compds. of formula I [A = (un)substituted C1-6 alkyl, (un)substituted C3-7 cycloalkyl, (un)substituted C3-6 alkenyl, (un)substituted C3-6 alkynyl, etc; R0 = H, (un)substituted C1-6 alkyl, etc; R1 = generic heteroarom. rings with proviso given; R2 = H, (un)substituted C1-6 alkyl, (un)substituted aryl, etc; R2, A = combined form 5-7 atom ring; R3, R4, R5 = H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, CN, NO2, C1-3 perfluoroalkyl, etc; R3, R4 = combined form ring of 3-7 carbon atoms or a heterocyclic ring contg. 1-3 heteroatoms; R6, R7 = H, (un)substituted C1-6 alkyl, etc; R8 = C(O)OR20, C(O)NR20R21, NR20R21, etc with proviso given; R7, R8 = combined form hetercyclic ring; R9, R9a = H, (un)substituted C1-6 alkyl, etc; R9, R9a = combined form carbocyclic ring of 3-7 atoms; R10, R10a = H, (un)substituted C1-6 alkyl, (un)substituted aryl, etc; R10, R10a = combined form carbocyclic ring of 3-7 atoms, double bond oxygen] useful as gonadotropin releasing hormone antagonists (no data), are prepd. For example, the title compd. II was prepd.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1997:511777 CAPLUS
DN 127:121742
TI Preparation of heterocyclic compounds as antagonists of gonadotropin releasing hormone
IN Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Girotra, Narindar N.; Lin, Peter; Wyvratt, Matthew J.
PA Merck & Co., Inc., USA; Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Girotra, Narindar N.; Lin, Peter; Wyvratt, Matthew J.
SO PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9721704	A1	19970619	WO 1996-US19444	19961210
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	AU 707641	B2	19990715		
				US 1995-8633P	P 19951214
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				WO 1996-US19444W	19961210
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			GB 1996-3242 A 19960216
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JP 2001106685	A2	20010417	JP 2000-257791 19961210
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			GB 1996-3242 A 19960216
			JP 1997-522124 A319961210
JP 3230818	B2	20011119	JP 1997-522124 19961210
			US 1995-8633P P 19951214
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AT 215081	E	20020415	AT 1996-944249 19961210
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			GB 1996-3242 A 19960216
ZA 9610536	A	19970814	ZA 1996-10536 19961213
			US 1995-8633P P 19951214
NO 9802729	A	19980813	NO 1998-2729 19980612
			US 1995-8633P P 19951214
			GB 1996-3242 A 19960216
			WO 1996-US19444W 19961210

PATENT FAMILY INFORMATION:

FAN 1998:479019

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5780437	A	19980714	US 1996-760816	19961205
	US 6200957	B1	20010313	US 1998-115497	19980714
				US 1995-8633P P	19951214
				US 1996-760816 A2	19961205

FAN 2000:68450

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000004013	A1	20000127	WO 1999-US15581	19990709

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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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			US 1995-8633P P 19951214
			US 1996-760816 A2 19961205
CA 2337407	AA	20000127	CA 1999-2337407 19990709
			US 1998-115497 A 19980714
			WO 1999-US15581W 19990709
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			WO 1999-US15581W 19990709

	EP 1095038	A1	20010502	EP 1999-933850	19990709
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				WO 1999-US15581W	19990709

FAN 2001:178434

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
				JP 1997-522124 A3	19961210
	ZA 9610536	A	19970814	ZA 1996-10536	19961213
				US 1995-8633P P	19951214
	CA 2337407	AA	20000127	CA 1999-2337407	19990709
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709
	WO 2000004013	A1	20000127	WO 1999-US15581	19990709
	W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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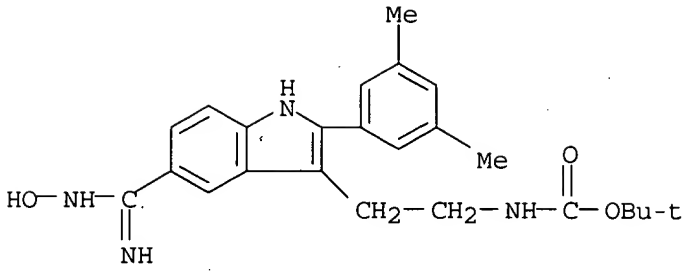
				WO 1999-US15581W	19990709
	EP 1095038	A1	20010502	EP 1999-933850	19990709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709
	JP 2002520409	T2	20020709	JP 2000-560119	19990709
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709

OS MARPAT 127:121742

IT **192644-10-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic compds. as antagonists of gonadotropin releasing hormone)

RN 192644-10-3 CAPLUS

CN Carbamic acid, [2-[2-(3,5-dimethylphenyl)-5-[(hydroxyamino)iminomethyl]-1H-indol-3-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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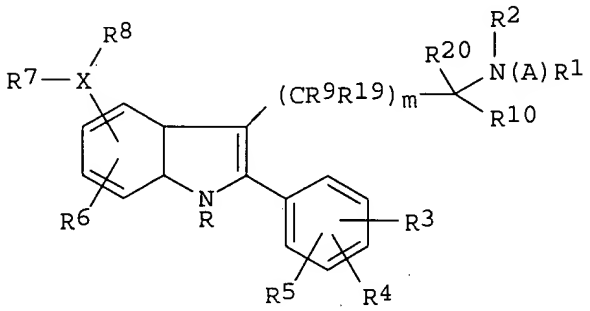

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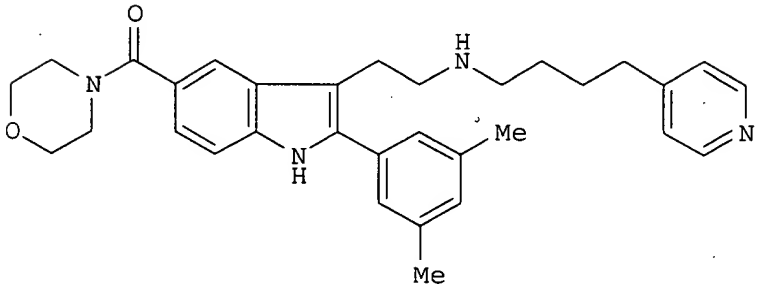
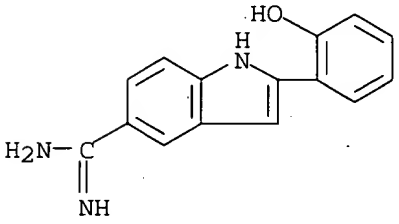


II

AB The title compds. I [A = alkyl, etc.; R = H, alkyl, etc.; R1 = heterocyclic ring (generic structures given); R2 = H, alkyl, etc.; or R2A = ring; R3, R4, R5 = H, (un)substituted alkyl, alkenyl, etc.; or R3R4 = ring; R6 = H, (un)substituted alkyl, etc.; R7 = H, (un)substituted alkyl; unless X is hydrogen or halo, then R7 is absent; R8 = heterocyclic ring, etc.; or R7R8 = heterocyclic ring; R9, R19 = H, (un)substituted alkyl; further details on R9R19 and R9A are given; R20, R10 = H, (un)substituted alkyl, etc.; further details on R20R10, and R9R20, R9R2, R20R2, R20A are given; m = 0 to 3; X = N, etc.], useful as antagonists of gonadotropin releasing hormone (no data), are prepd. I may be useful for the treatment of a variety of sex-hormone related and other conditions in both men and women. The title compd. II was prepd. in a multistep process.

L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1996:398902 CAPLUS
DN 125:131628
TI Derivatives of 5-amidine indole as inhibitors of thrombin catalytic

activity
AU Iwanowicz, Edwin J.; Lau, Wan F.; Lin, James; Roberts, Daniel G. M.; Seiler, Steven M.
CS Bristol-Myers Squibb Pharmaceutical Res. Inst., Princeton, NJ, 08543-4000, USA
SO Bioorganic & Medicinal Chemistry Letters (1996), 6(12), 1339-1344
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
IT **179748-10-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of derivs. of 5-amidine indole as inhibitors of thrombin catalytic activity and structure-activity relations)
RN 179748-10-8 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(2-hydroxyphenyl)- (9CI) (CA INDEX NAME)



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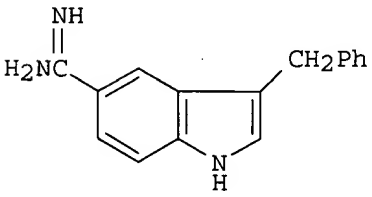
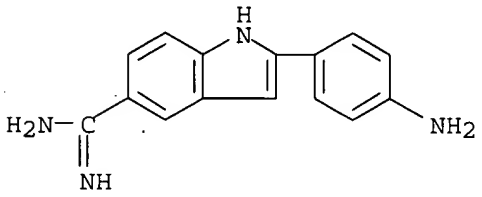


I

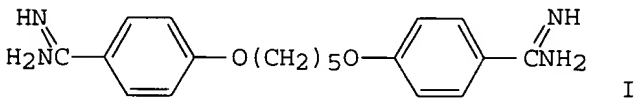
AB Substituted 5-amidine indoles were constructed based upon a computational anal. of putative modes of binding to thrombin utilizing coordinates from the crystal structure of BMS-183,507-.alpha.-thrombin complex. These analogs display competitive kinetics for the inhibition of human .alpha.-thrombin. Structure-activity relations are discussed. The most potent member of this series I, shows marked potency for thrombin with an inhibition const., Ki of 260 nM.

L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS
AN 1985:346 CAPLUS
DN 102:346
TI Hypotensive effect of aromatic amidines and imidazolines
AU Bielenberg, G. W.; Krieglstein, J.
CS Inst. Pharmakol. Toxikol., Philipps-Univ., Marburg/Lahn, 3550, Fed. Rep.

Ger.
SO Arzneimittel-Forschung (1984), 34(9), 958-67
CODEN: ARZNAD; ISSN: 0004-4172
DT Journal
LA German
IT **93490-78-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihypertensive activity of)
RN 93490-78-9 CAPLUS
CN 1H-Indole-5-carboximidamide, 2-(4-aminophenyl)- (9CI) (CA INDEX NAME)



GI



I

AB Of 16 arom. amidines or imidazolines tested for hypotensive activity in exptl. animals, all substances, except for 5-amidino-2-phenylindole (271/179) [93490-77-8], caused a dose-dependent hypotensive effect. Pentamidine (I) [100-33-4] was one of the most effective hypotensives. The biscationic character of a compd. was a prerequisite for strong antihypertensive activity. The antihypertensive activity of the most active compds. appeared to have a peripheral origin and did not appear to be mediated via parasympathomimetic or histaminic mechanisms. Cardiovascular effects of these compds. are also given. The antihypertensive activity of these compds. is discussed in terms of a musculotropic action on vascular smooth muscle.

=> d his

(FILE 'HOME' ENTERED AT 12:03:41 ON 13 JUN 2003)

FILE 'REGISTRY' ENTERED AT 12:03:57 ON 13 JUN 2003
L1 STRUCTURE UPLOADED
L2 6 S L1
L3 119 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 12:05:23 ON 13 JUN 2003
L4 19 S L3

```
=> d cost
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CONNECT CHARGES                                   1.36       2.19
NETWORK CHARGES                                   0.24       0.42
SEARCH CHARGES                                    0.00     147.75
DISPLAY CHARGES                                 110.83     110.83
                                                -------    -------
                                                112.43     261.19
CAPLUS FEE (5%)                                   5.61       5.61
                                                -------    -------
FULL ESTIMATED COST                             118.04     266.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                             -12.37     -12.37

IN FILE 'CAPLUS' AT 12:07:39 ON 13 JUN 2003
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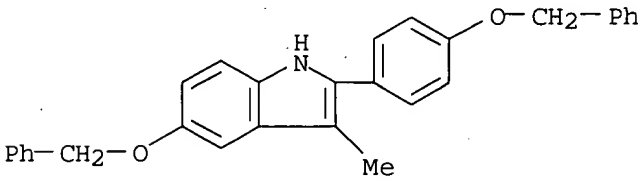
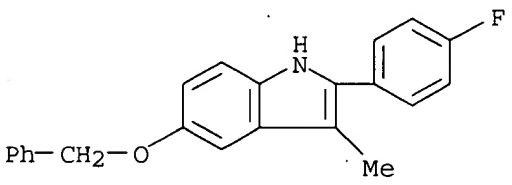
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N-benzyl-2-phenylindoles as estrogenic agents)
RN 198479-63-9 CAPLUS
CN 1H-Indole, 3-methyl-5-(phenylmethoxy)-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



IT **198479-64-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-benzyl-2-phenylindoles as estrogenic agents)
RN 198479-64-0 CAPLUS
CN 1H-Indole, 2-(4-fluorophenyl)-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I or II; R1 = H, OH, C14 esters or alkyl ethers, halo; R2-R6 = H, OH, halo, etc. (with the proviso that, when R1 is H, R2 is not OH); n = 2-3; X = H, CN, NO2, etc.; Z = CH:CHC(O)Y, C.tplbond.C(CH2)nY; Y = NR7R8 (wherein R7, R8 = H, C1-6 alkyl, Ph; R7R8 = (CH2)p; p = 2-6), a (un)satd. 5-7 membered **heterocycle**, a bicyclic ring system], useful as estrogenic agents for treating or preventing bone loss, disease states or syndromes which are caused or assocd. with an estrogen deficiency, and cardiovascular disease, were prepd. by reacting the **indole** III with an acrylamide H2C:CHC(O)Y or by reacting the **indole** IV with HC.tplbond.C(CH2)nY. Thus, compd. (E)-I [R1, R4 = OH; R2, R3, R5, R6 = H; X = Me; Z = CH:CHC(O)NHtBu] showed RBA (17.beta.-estradiol = 100) of 40.

L10 ANSWER 28 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1997:701837 CAPLUS
DN 127:358782

TI Preparation of 2-phenyl-1-[4-(2-aminoethoxy)benzyl]**indoles** as estrogenic agents
IN Miller, Chris P.; Tran, Bach D.; Collini, Michael D.
PA American Home Products Corporation, USA
SO Eur. Pat. Appl., 85 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

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				US 1997-833271 A	19970404
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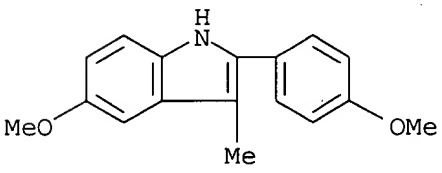
OS MARPAT 127:358782

IT **91444-18-7P 198479-60-6P 198479-61-7P**
198479-62-8P 198479-63-9P 198479-64-0P
198479-65-1P 198479-66-2P 198479-67-3P
198479-68-4P 198479-69-5P 198479-70-8P
198479-71-9P 198479-72-0P 198479-73-1P
198479-74-2P 198479-75-3P 198479-76-4P
198480-99-8P 198481-07-1P 198481-12-8P
198481-34-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 2-phenyl-1-[4-(2-aminoethoxy)benzyl]**indoles** as estrogenic agents)

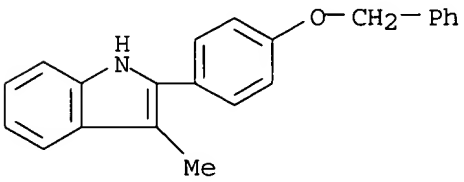
RN 91444-18-7 CAPLUS

CN 1H-Indole, 5-methoxy-2-(4-methoxyphenyl)-3-methyl- (9CI) (CA INDEX NAME)



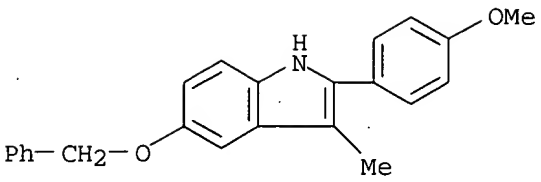
RN 198479-60-6 CAPLUS

CN 1H-Indole, 3-methyl-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 198479-61-7 CAPLUS

CN 1H-Indole, 2-(4-methoxyphenyl)-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 198479-62-8 CAPLUS
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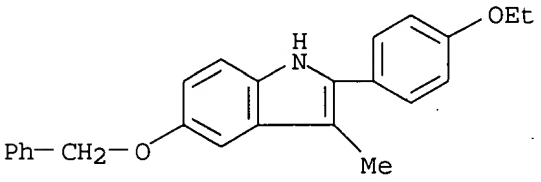
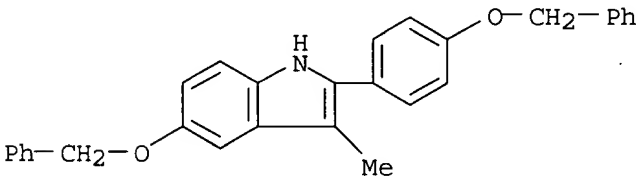


RN 198479-63-9 CAPLUS
CN 1H-Indole, 3-methyl-5-(phenylmethoxy)-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 198479-64-0 CAPLUS
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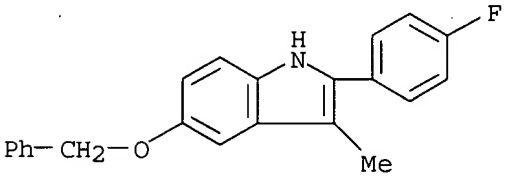
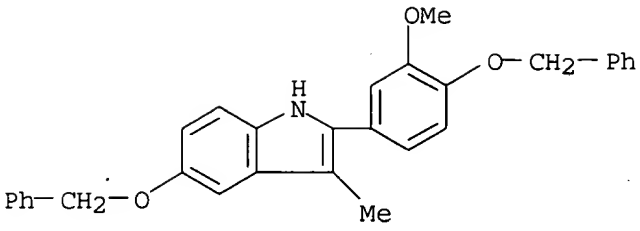


RN 198479-65-1 CAPLUS
CN 1H-Indole, 2-[3-methoxy-4-(phenylmethoxy)phenyl]-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 198479-66-2 CAPLUS
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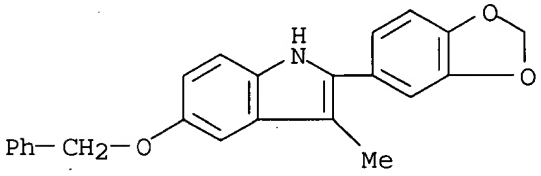
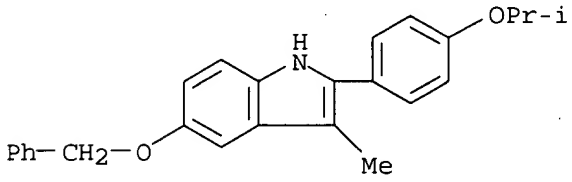
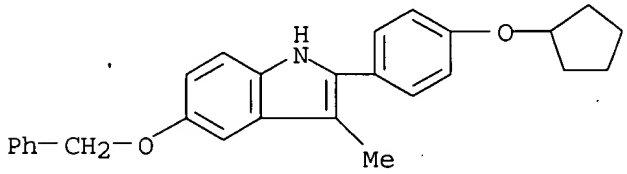


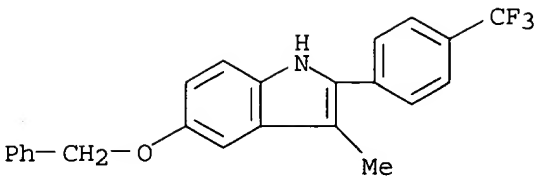
RN 198479-67-3 CAPLUS
CN 1H-Indole, 3-methyl-2-[4-(1-methylethoxy)phenyl]-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



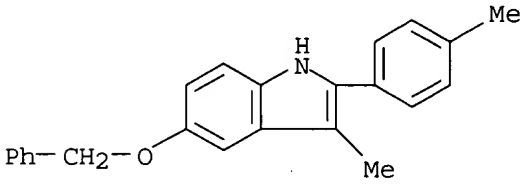
RN 198479-68-4 CAPLUS
CN 1H-Indole, 2-[4-(cyclopentyloxy)phenyl]-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



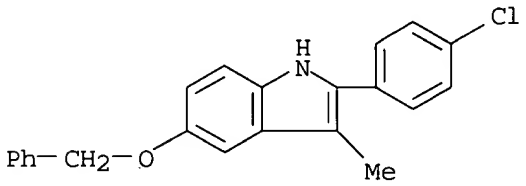
RN 198479-69-5 CAPLUS
CN 1H-Indole, 3-methyl-5-(phenylmethoxy)-2-[4-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



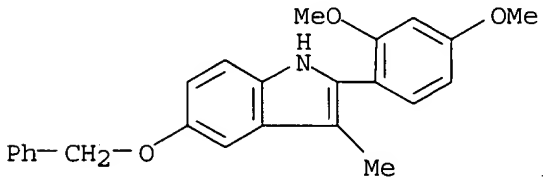
RN 198479-70-8 CAPLUS
CN 1H-Indole, 3-methyl-2-(4-methylphenyl)-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



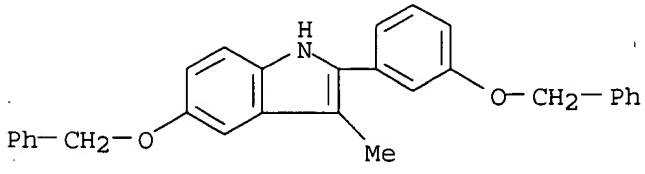
RN 198479-71-9 CAPLUS
CN 1H-Indole, 2-(4-chlorophenyl)-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

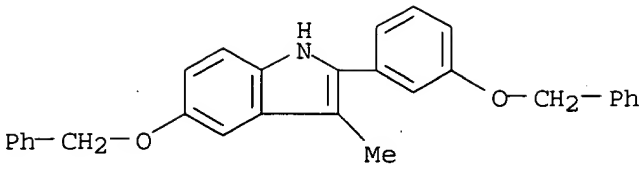


RN 198479-72-0 CAPLUS
CN 1H-Indole, 2-(2,4-dimethoxyphenyl)-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)

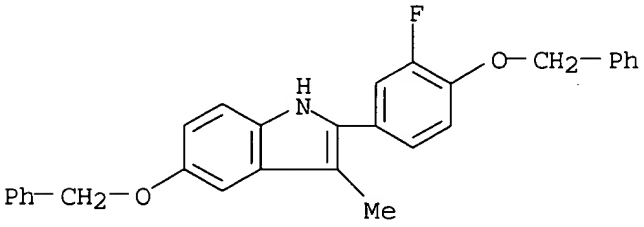


RN 198479-73-1 CAPLUS
CN 1H-Indole, 3-methyl-5-(phenylmethoxy)-2-[3-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)

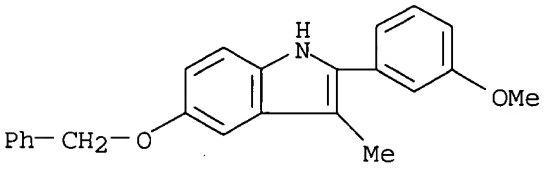




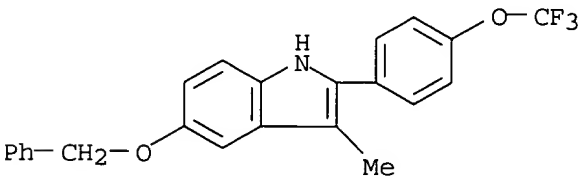
RN 198479-74-2 CAPLUS
CN 1H-Indole, 2-[3-fluoro-4-(phenylmethoxy)phenyl]-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



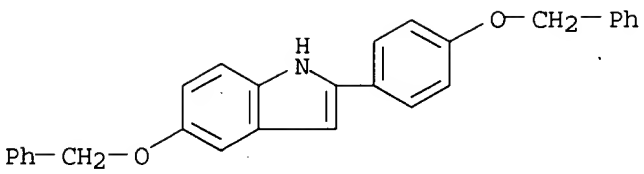
RN 198479-75-3 CAPLUS
CN 1H-Indole, 2-(3-methoxyphenyl)-3-methyl-5-(phenylmethoxy)- (9CI) (CA INDEX NAME)



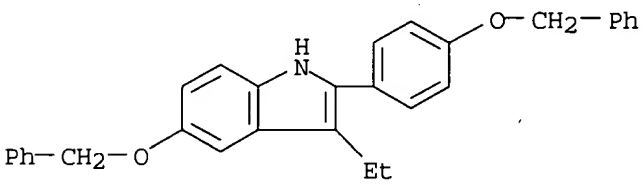
RN 198479-76-4 CAPLUS
CN 1H-Indole, 3-methyl-5-(phenylmethoxy)-2-[4-(trifluoromethoxy)phenyl]- (9CI) (CA INDEX NAME)



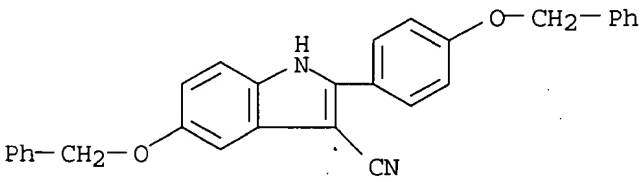
RN 198480-99-8 CAPLUS
CN 1H-Indole, 5-(phenylmethoxy)-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



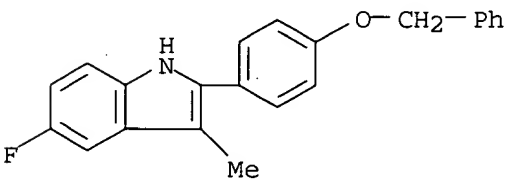
RN 198481-07-1 CAPLUS
CN 1H-Indole, 3-ethyl-5-(phenylmethoxy)-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 198481-12-8 CAPLUS
CN 1H-Indole-3-carbonitrile, 5-(phenylmethoxy)-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 198481-34-4 CAPLUS
CN 1H-Indole, 5-fluoro-3-methyl-2-[4-(phenylmethoxy)phenyl]- (9CI) (CA INDEX NAME)



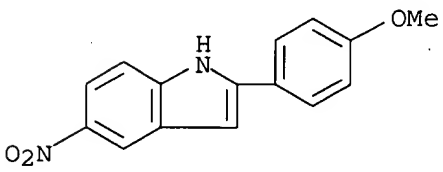
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

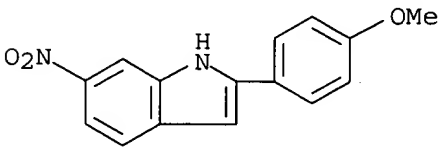
AB The title compds. [I or II; R1 = H, OH, C1-12 ester, etc.; R2-R6 = H, OH, C1-6 alkyl, etc.; X = H, C1-6 alkyl, CN, etc.; n = 2-3; Y = NR7R8 (wherein R7, R8 = H, C1-6 alkyl, (un)substituted Ph; R7R8 = (CH2)p; p = 2-6), 5-7 membered (un)satd. **heterocycle**, C6-12 bicyclic

AB Title compds. [I; ABCD = CH:CHCH:CH, CH2CH2CH2CO, CH2CH2COCH2, O2CCH2CH2, N:CHCH:N, SCH:N, N:NNH, etc.; R1 = SO2Me, SO2NH2, SO2NHCOF3, POMENH2, SONHNH2, etc.; R2 = H, halo, alkoxy, alkylthio, cyano, CF3, N3, CO2H, alkoxycarbonyl, alkyl, cycloalkyl, (substituted) Ph, naphthyl, mono- or disubstituted heteroaryl, etc.; R3, R4 = H, CF3, cyano, alkyl, CO2H, etc.], were prepd. Thus, 2-phenoxy-1-(4-methylthiophenyl)ethanone (prepn. given) was heated 2 h in polyphosphoric acid at 70.degree. to give 3-(4-methylthiophenyl)benzo[b]furan. This was refluxed with NBS and benzoyl peroxide in CCl4 under a spotlight to give 2-bromo-3-(4-methylthiophenyl)benzo[b]furan. The latter was treated with phenylboric acid, Pd(PPh3)4, and NaOH in PhMe/EtOH at reflux for 20 h to give 3-(4-methylthiophenyl)-2-phenylbenzo[b]furan, which was oxidized to title compd. (II) using monoperoxyphthalic acid in CH2Cl2/MeOH. II at 100 nM inhibited cyclooxygenase-2 and -1 by 94% and 0%, resp.

L10 ANSWER 32 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1996:331929 CAPLUS
DN 125:114547
TI Structure-activity relationships of benzimidazoles and related **heterocycles** as topoisomerase I poisons
AU Kim, Jung Sun; Sun, Qun; Gatto, Barbara; Yu, Chiang; Liu, Angela; Liu, Leroy F.; LaVoie, Edmond J.
CS Department of Pharmaceutical Chemistry, Rutgers, The State University of New Jersey, Piscataway, NJ, 08855, USA
SO Bioorganic & Medicinal Chemistry (1996), 4(4), 621-630
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
IT **178970-27-9P 178970-28-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of (methoxyphenyl)benzimidazoles and analogs as topoisomerase inhibitors)
RN 178970-27-9 CAPLUS
CN 1H-Indole, 2-(4-methoxyphenyl)-5-nitro- (9CI) (CA INDEX NAME)

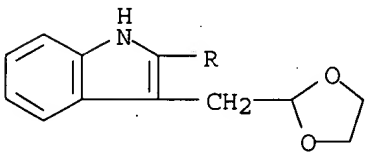


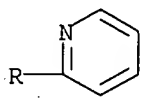
RN 178970-28-0 CAPLUS
CN 1H-Indole, 2-(4-methoxyphenyl)-6-nitro- (9CI) (CA INDEX NAME)



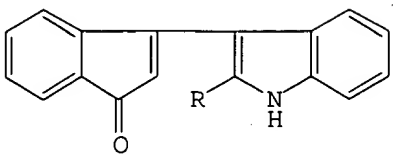
AB A series of substituted 2-(4-methoxyphenyl)-1H-benzimidazoles were synthesized and evaluated as inhibitors of topoisomerase I. The presence of a 5-formyl-, 5-(aminocarbonyl)-, or 5-nitro group (i.e., substituents capable of acting as hydrogen bond acceptors) correlated with the potential of select derivs. to inhibit topoisomerase I. In contrast to bi- and terbenzimidazoles, the substituted benzimidazoles that were active as topoisomerase I poisons exhibited min. or no DNA binding affinity. 5-Nitro-2-(4-methoxyphenyl)-1H-benzimidazole exhibited the highest activity and was significantly more active than the 4-nitro positional isomer. The 5- and 6-nitro derivs. of 2-(4-methoxyphenyl)benzoxazole, 2-(4-methoxyphenyl)benzothiazole, and 2-(4-methoxyphenyl)**indole** were synthesized and their relative activity as topoisomerase I inhibitors detd. None of these heterocyclic analogs were effective in significantly inhibiting cleavable-complex formation in the presence of DNA and topoisomerase I, suggesting a high degree of structural specificity assocd. with the interaction of these substituted benzimidazoles with the enzyme or the enzyme-DNA complex. In evaluating their cytotoxicity, these new topoisomerase I poisons also exhibited no significant cross-resistance against cell lines that express camptothecin-resistant topoisomerase I.

L10 ANSWER 33 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1996:327557 CAPLUS
DN 125:58819
TI Low-valent titanium induced **indole** formation: syntheses of secofascaplysin, indolopyridocoline and an endothelin-receptor-antagonist
AU Fuerstner, Alois; Ernst, Andreas; Krause, Helga; Ptock, Arne
CS Max-Planck-Inst. Kohlenforschung, Muelheim/Ruhr, D-45470, Germany
SO Tetrahedron (1996), 52(21), 7329-7344
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier
DT Journal
LA English
OS CASREACT 125:58819
IT **178210-63-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(low-valent titanium induced **indole** formation in the syntheses of secofascaplysin, indolopyridocoline and an endothelin receptor antagonist)
RN 178210-63-4 CAPLUS
CN 1H-Indole, 3-(1,3-dioxolan-2-ylmethyl)-2-(2-pyridinyl)- (9CI) (CA INDEX NAME)

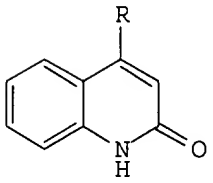




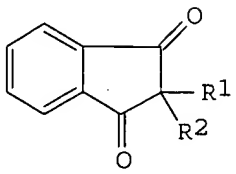
IT **178210-65-6P 178210-66-7P 178210-67-8P**



II



III



IV

AB Treating indan-1,3-dione (I) with **indole**, 2-phenylindole, antipyrine, 4-aminoantipyrine and 3-amino-1-phenylpyrazol-2-in-5-one gave addn. at C-1; thus, treating I with **indole** gave 82% II (R = H), whose Schmidt reaction gave carbostyrile III. Alkylation of I with gramine methosulfate and skatyl bromide occurred at C-2 to give IV (R1 = R2 = 3-indolylmethyl; R1 = H, R2 = 3-indolylmethy), resp. Condensing I with 3-formylindole gave IV (R1R2 = 3-indolmethylene), whose treatment with Me2NH gave IV (R1 = H, R2 = .alpha.-dimethylamino-3-indolylmethyl).

L10 ANSWER 43 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1992:426337 CAPLUS
DN 117:26337
TI Preparation and formulation of 2-phenylindole derivatives as lipoxygenase inhibitors
IN Hasegawa, Yukio; Suzuki, Yasushi; Sato, Michitaka; Yamamoto, Norio; Hasumi, Kohichi; Shitara, Kazuhiro; Miyasaka, Katsuhiko; Mikami, Takashi; Miyazawa, Katsuhiko; et al.
PA Teikoku Hormone Mfg. Co., Ltd., Japan
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9202500	A1	19920220	WO 1991-JP1000	19910725
	W: AU, CA, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
				JP 1990-201142	19900731
				JP 1990-233094	19900905
	AU 9182259	A1	19920302	AU 1991-82259	19910725
				JP 1990-201142	19900731
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				WO 1991-JP1000	19910725
	JP 2988723	B2	19991213	JP 1991-512380	19910725
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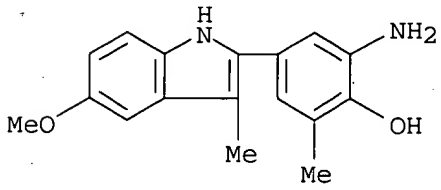
				WO 1991-JP1000	19910725

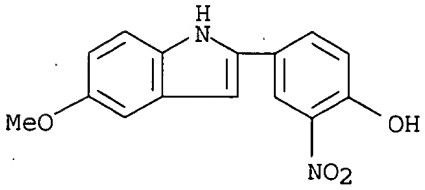
OS MARPAT 117:26337
IT **141771-84-8P 141771-85-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, in prepn. of antiallergic agent)
RN 141771-84-8 CAPLUS
CN Phenol, 2-amino-4-(5-methoxy-3-methyl-1H-indol-2-yl)-6-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

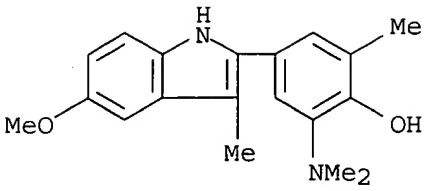


● HCl

RN 141771-85-9 CAPLUS
CN Phenol, 4-(5-methoxy-1H-indol-2-yl)-2-nitro- (9CI) (CA INDEX NAME)

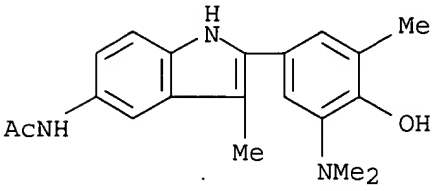


IT **141771-95-1P 141771-96-2P 141771-97-3P**
141771-98-4P 141772-00-1P 141772-01-2P
141772-02-3P 141772-03-4P 141772-05-6P
141772-06-7P 141772-07-8P 141772-08-9P
141772-09-0P 141772-11-4P 141772-12-5P
141772-13-6P 141772-14-7P 141772-15-8P
141772-16-9P 141772-17-0P 141772-18-1P
141772-19-2P 141772-20-5P 141772-21-6P
141772-22-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as lipoxygenase inhibitor)
RN 141771-95-1 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(5-methoxy-3-methyl-1H-indol-2-yl)-6-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



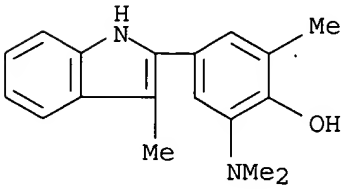
● HCl

RN 141771-96-2 CAPLUS
CN Acetamide, N-[2-[3-(dimethylamino)-4-hydroxy-5-methylphenyl]-3-methyl-1H-indol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



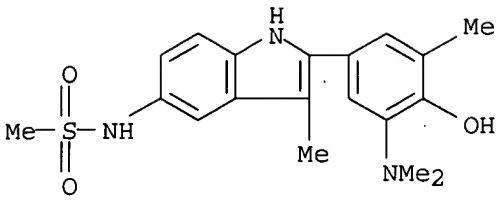
● HCl

RN 141771-97-3 CAPLUS
CN Phenol, 2-(dimethylamino)-6-methyl-4-(3-methyl-1H-indol-2-yl)-, dihydrochloride (9CI) (CA INDEX NAME)



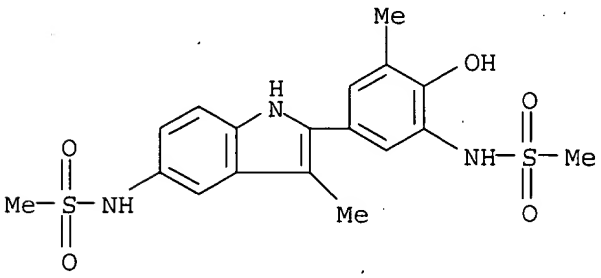
●2 HCl

RN 141771-98-4 CAPLUS
CN Methanesulfonamide, N-[2-[3-(dimethylamino)-4-hydroxy-5-methylphenyl]-3-methyl-1H-indol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

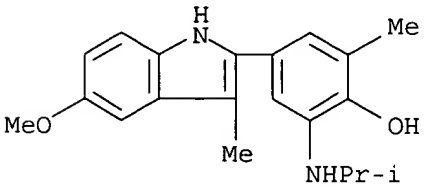


● HCl

RN 141772-00-1 CAPLUS
CN Methanesulfonamide, N-[2-hydroxy-3-methyl-5-[3-methyl-5-[(methylsulfonyl)amino]-1H-indol-2-yl]phenyl]- (9CI) (CA INDEX NAME)

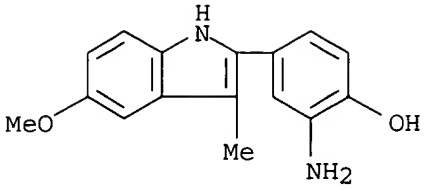


RN 141772-01-2 CAPLUS
CN Phenol, 4-(5-methoxy-3-methyl-1H-indol-2-yl)-2-methyl-6-[(1-methylethyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)



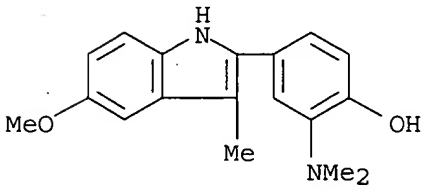
● HCl

RN 141772-02-3 CAPLUS
CN Phenol, 2-amino-4-(5-methoxy-3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



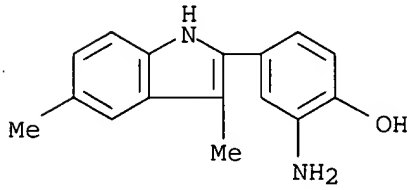
● HCl

RN 141772-03-4 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(5-methoxy-3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



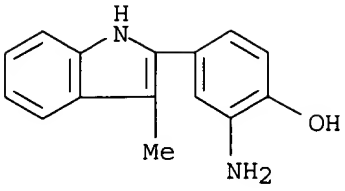
● HCl

RN 141772-05-6 CAPLUS
CN Phenol, 2-amino-4-(3,5-dimethyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



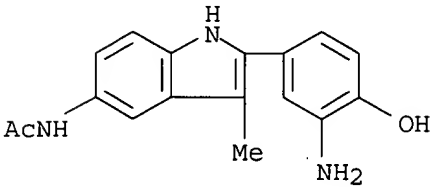
● HCl

RN 141772-06-7 CAPLUS
CN Phenol, 2-amino-4-(3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



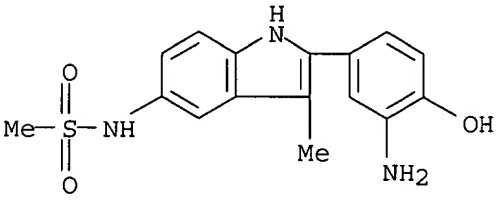
● HCl

RN 141772-07-8 CAPLUS
CN Acetamide, N-[2-(3-amino-4-hydroxyphenyl)-3-methyl-1H-indol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

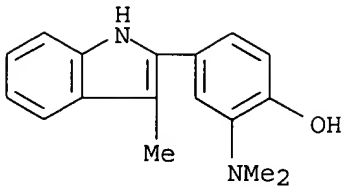


● HCl

RN 141772-08-9 CAPLUS
CN Methanesulfonamide, N-[2-(3-amino-4-hydroxyphenyl)-3-methyl-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

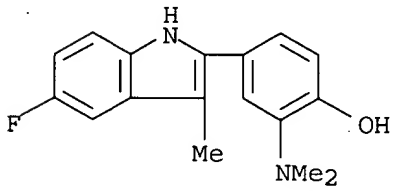


RN 141772-09-0 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



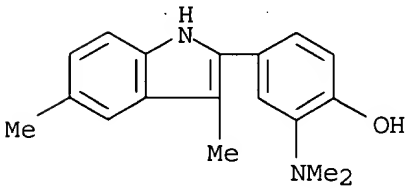
● HCl

RN 141772-11-4 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(5-fluoro-3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



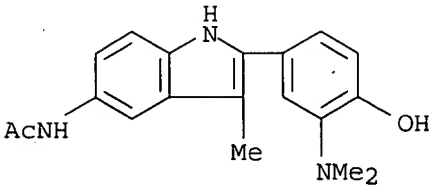
● HCl

RN 141772-12-5 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(3,5-dimethyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

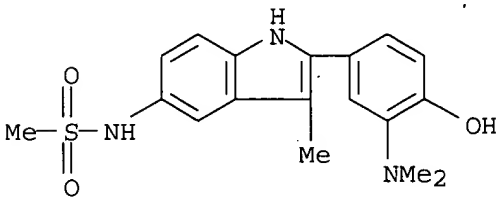


● HCl

RN 141772-13-6 CAPLUS
CN Acetamide, N-[2-[3-(dimethylamino)-4-hydroxyphenyl]-3-methyl-1H-indol-5-yl]- (9CI) (CA INDEX NAME)

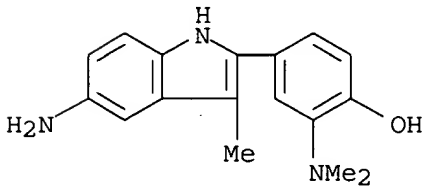


RN 141772-14-7 CAPLUS
CN Methanesulfonamide, N-[2-[3-(dimethylamino)-4-hydroxyphenyl]-3-methyl-1H-indol-5-yl]-, monohydrochloride (9CI) (CA INDEX NAME)



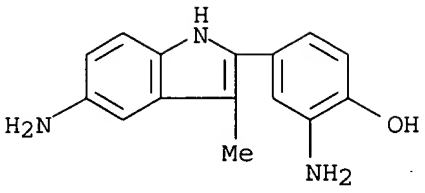
● HCl

RN 141772-15-8 CAPLUS
CN Phenol, 4-(5-amino-3-methyl-1H-indol-2-yl)-2-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)



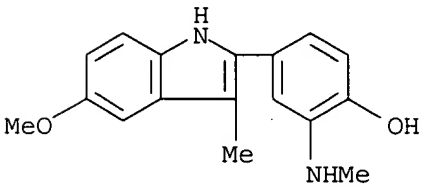
● HCl

RN 141772-16-9 CAPLUS
CN Phenol, 2-amino-4-(5-amino-3-methyl-1H-indol-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

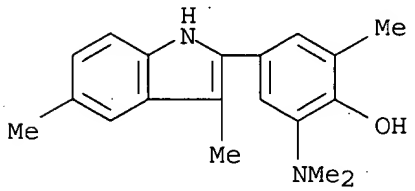


● HCl

RN 141772-17-0 CAPLUS
CN Phenol, 4-(5-methoxy-3-methyl-1H-indol-2-yl)-2-(methylamino)- (9CI) (CA INDEX NAME)

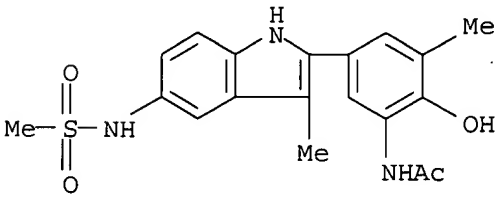


RN 141772-18-1 CAPLUS
CN Phenol, 2-(dimethylamino)-4-(3,5-dimethyl-1H-indol-2-yl)-6-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

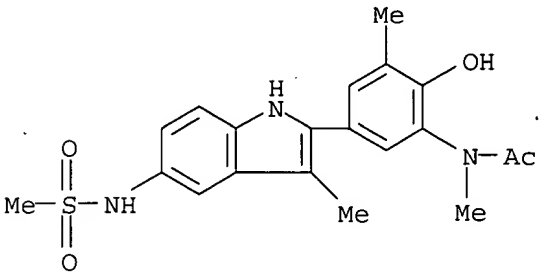


● HCl

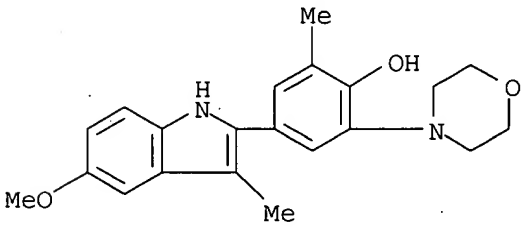
RN 141772-19-2 CAPLUS
CN Acetamide, N-[2-hydroxy-3-methyl-5-[3-methyl-5-[(methylsulfonyl)amino]-1H-indol-2-yl]phenyl]- (9CI) (CA INDEX NAME)



RN 141772-20-5 CAPLUS
CN Acetamide, N-[2-hydroxy-3-methyl-5-[3-methyl-5-[(methylsulfonyl)amino]-1H-indol-2-yl]phenyl]-N-methyl- (9CI) (CA INDEX NAME)

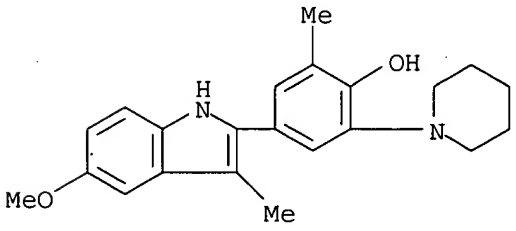


RN 141772-21-6 CAPLUS
CN Phenol, 4-(5-methoxy-3-methyl-1H-indol-2-yl)-2-methyl-6-(4-morpholinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

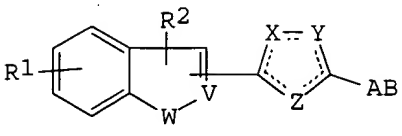
RN 141772-22-7 CAPLUS
CN Phenol, 4-(5-methoxy-3-methyl-1H-indol-2-yl)-2-methyl-6-(1-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

GI

GI



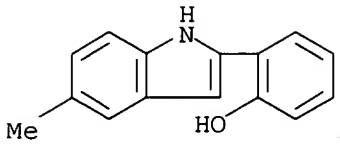
I

AB Title compds. I [X, Y, Z = O, S, N, C and at least one of X, Y, and Z = O, S, N; the dotted circle = one or two double bonds in any position; R1 = H, OH, alkyl, alkenyl, alkynyl, amino, cyano, etc.; R2 = H, halo, alkyl, alkoxy, alkylcarbonyl; V = CH, C (when bond with the 5-membered ring); W = O, S, NR3 (R3 = H, alkyl, alkenyl, alkynyl); A = bond, (substituted) alkylene; B = non-arom. aza(bi)cyclyl, NR4R5 (R4, R5 = H, alkyl, alkenyl, alkynyl, aralkyl)] are prepd. I are useful for treating psychotic disorders (e.g. schizophrenia, mania), anxiety, alc. or drug withdrawal, pain, gastric stasis, gastric dysfunction (e.g. peptic ulcer, esophageal reflux, flatulence), migraine, nausea, vomiting, and presenile and senile dementia (Alzheimer's disease) (no data). A mixt. of H2NOH, HCl, K2CO3, and 1-methylindole-3-nitrile in EtOH was refluxed to give 1-methylindol-3-ylamide oxime, which in DMF in the presence of mol. sieves was successively treated with NaH and 3-carbomethoxy-1-azabicyclo[2.2.2]octane to give 3-[3-(methylindol-3-yl)-1,2,4-oxadiazol-5-yl]-1-azabicyclo[2.2.2]octane.

L10 ANSWER 48 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1989:85613 CAPLUS
DN 110:85613
TI Thermal recording material using chromeno compound for improved resistance to IR radiation
IN Kanda, Nobuo; Abe, Yukihiro; Kondo, Mitsuru
PA Kanzaki Paper Mfg. Co., Ltd., Japan
SO. Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 273418	A2	19880706	EP 1987-119234	19871224
	EP 273418	A3	19900418		
	EP 273418	B1	19931124		
	R: DE, FR, GB				
				JP 1986-314744	19861227
	JP 63166588	A2	19880709	JP 1986-314744	19861227
	US 4803193	A	19890207	US 1987-137368	19871223
				JP 1986-314744	19861227

OS CASREACT 110:85613
IT **118234-55-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, chromeno compd. from, for thermal recording material)
RN 118234-55-2 CAPLUS
CN Phenol, 2-(5-methyl-1H-indol-2-yl)- (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.

AB A thermal recording material contains a colorless dye I [Z = N-contg. 5-membered ring which may have an attached benzene ring and substituents; R1-R4 = H, C1-12 alkyl, C3-C12 alkenyl or alkynyl, C5-12 cycloalkyl, Ph, Ph-C1-2 alkyl, naphthyl; R1-R4 may form a part of a **heterocycle**] and a dye developer. The developer may be selected from polyvalent metal salts of arom. carboxylic acids. The above compn. may also contain an arom. diamine compd. The compn. forms images readable by optical character-reading devices. Thus, 3,6-bis(diethylamino)fluorenone was reacted with 2-(2-hydroxyphenyl)**indole** to obtain 3,6-bis(diethylamino)spiro[fluorene-9,6'-6'-H-chromeno(4,3-b)**indole**] (II). Three different dispersions of II, 4,4'-isopropylidenediphenol, and stearic acid amide in aq. Me cellulose were mixed and used to form thermal recording papers. The papers produced images which were stable against heat, IR radiation, and humidity and had high d.

L10 ANSWER 49 OF 52 CAPLUS COPYRIGHT 2003 ACS

AN 1988:590304 CAPLUS

DN 109:190304

TI Fused **heterocycles** from o-acylbenzenethiol derivatives

AU McKinnon, David M.; Lee, Kingsley R.

CS Chem. Dep., Univ. Manitoba, Winnipeg, MB, R3T 2N2, Can.

SO Canadian Journal of Chemistry (1988), 66(6), 1405-9
CODEN: CJCHAG; ISSN: 0008-4042

DT Journal

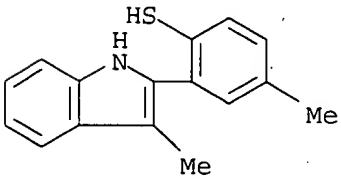
LA English

OS CASREACT 109:190304

IT **117136-97-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and attempted cyclization of)

RN 117136-97-7 CAPLUS

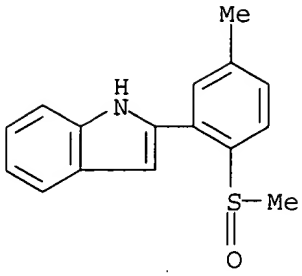
CN Benzenethiol, 4-methyl-2-(3-methyl-1H-indol-2-yl)- (9CI) (CA INDEX NAME)



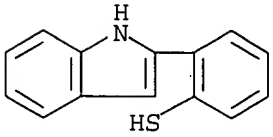
IT **117136-98-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, with hydrogen chloride)

RN 117136-98-8 CAPLUS

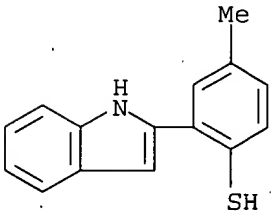
CN 1H-Indole, 2-[5-methyl-2-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)



IT **117136-95-5P 117136-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, with iodine)
RN 117136-95-5 CAPLUS
CN Benzenethiol, 2-(1H-indol-2-yl)- (9CI) (CA INDEX NAME)



RN 117136-96-6 CAPLUS
CN Benzenethiol, 2-(1H-indol-2-yl)-4-methyl- (9CI) (CA INDEX NAME)



IT **117136-92-2P 117136-94-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and demethylation of, with sodium in ammonia)
RN 117136-92-2 CAPLUS
CN 1H-Indole, 2-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)

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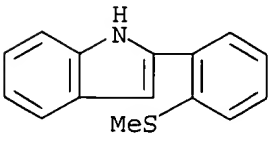
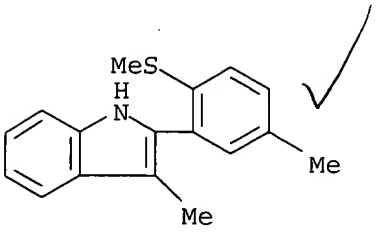


RN 117136-94-4 CAPLUS

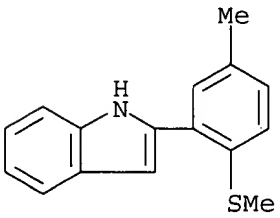
CN 1H-Indole, 3-methyl-2-[5-methyl-2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



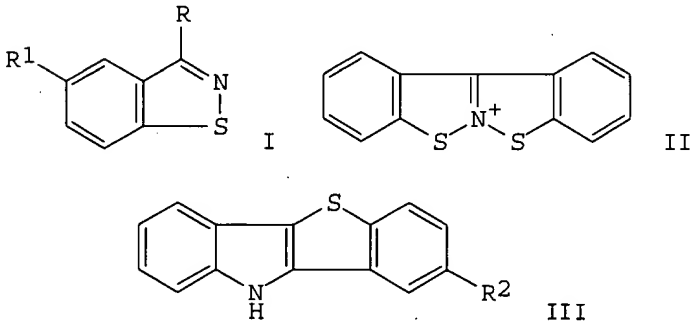
IT **117136-93-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., demethylation, and S-oxidn. of)

RN 117136-93-3 CAPLUS

CN 1H-Indole, 2-[5-methyl-2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



GI



AB The oximes of 2-acylthioanisole derivs. 2,5-MeS(R1)C6H3COR (R = Me, Et, Ph, 2-MeSC6H4; R1 = H, Me) may be conveniently converted into 1,2-benzisothiazoles I Ac2O in pyridine. I (R = 2-MeSC6H4, R1 = H), prepd. by this method, was further converted into the 1,2-benzisothiazolo[2,3-b]-1,2-benzisothiazolium system II. The phenylhydrazones of certain 2-acylthioanisoles are also cyclized by polyphosphoric acid to 2-(2-methylthio)phenylindoles, which are further converted into benzo[b]thieno[3,2-b]**indoles** III (R2 = H, Me) by demethylation and oxidn.

L10 ANSWER 50 OF 52 CAPLUS COPYRIGHT 2003 ACS

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NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
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NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
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NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
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NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA

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 NEWS 41   May 19  RAPRA enhanced with new search field, simultaneous left and
                   right truncation
 NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43   Jun 06  PASCAL enhanced with additional data

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 STRUCTURE UPLOADED

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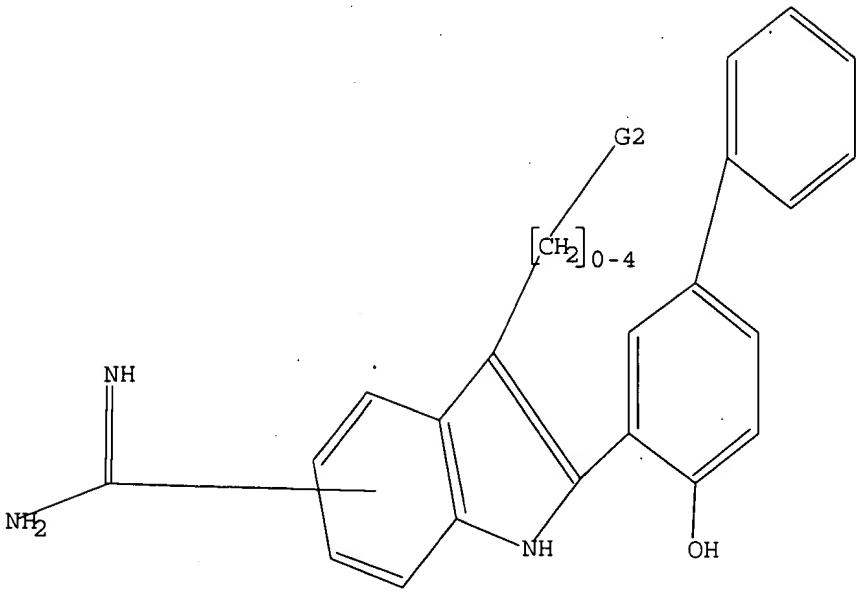
L1 HAS NO ANSWERS
L1 STR



G1

G2 C,H,Cb,Ak,Cy

G3 X,CH2,OH,PhO,COOH,NH,NH2,P

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 12:24:39 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:24:47 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 71 TO ITERATE

100.0% PROCESSED 71 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	148.95	149.16

STN INTERNATIONAL LOGOFF AT 12:24:53 ON 13 JUN 2003

Welcome to STN International! Enter x:x

LOGINID:ssspta1611sxp

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA

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 NEWS 41   May 19  RAPRA enhanced with new search field, simultaneous left and
                   right truncation
 NEWS 42   Jun 06  Simultaneous left and right truncation added to CBNB
 NEWS 43   Jun 06  PASCAL enhanced with additional data

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

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  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

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COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.42       0.42

FILE 'REGISTRY' ENTERED AT 11:33:30 ON 13 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   11 JUN 2003  HIGHEST RN 529474-19-9
DICTIONARY FILE UPDATES:  11 JUN 2003  HIGHEST RN 529474-19-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 STRUCTURE UPLOADED

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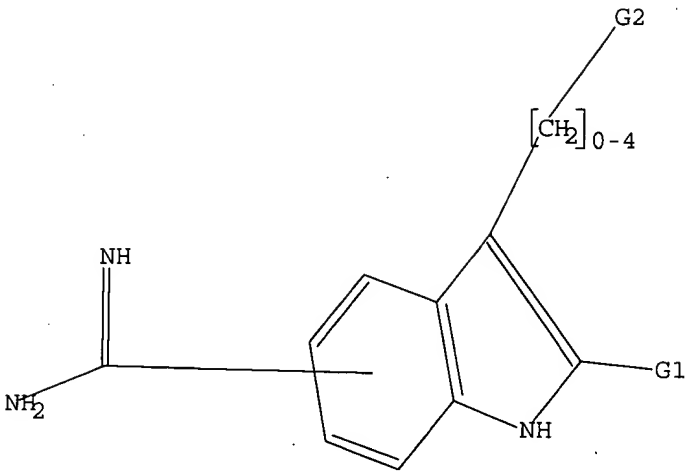
L1 HAS NO ANSWERS
L1 STR



G1 Cb,Cy,Hy
G2 C,H,Cb,Ak,Cy

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 11:36:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3719 TO ITERATE

26.9% PROCESSED 1000 ITERATIONS 6 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 70724 TO 78036
PROJECTED ANSWERS: 163 TO 729

L2 6 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:36:22 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 73093 TO ITERATE

100.0% PROCESSED 73093 ITERATIONS 181 ANSWERS
SEARCH TIME: 00.00.12

L3 181 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	149.75	150.17

FILE 'CAPLUS' ENTERED AT 11:36:41 ON 13 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 13 Jun 2003 VOL 138 ISS 25
FILE LAST UPDATED: 12 Jun 2003 (20030612/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 737 L3

=> s l4 and heterocycle
L5 4 L4 AND HETEROCYCLE

=> d l5 fbib hitstr abs total

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 2000:68450 CAPLUS
DN 132:107953
TI Preparation of heterocyclic compounds as antagonists of gonadotropin releasing hormone
IN Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Lin, Peter; Ponpipom, Mitree M.; Wyvratt, Matthew J.; Girotra, Narindar N.; Young, Jonathan
PA Merck and Co., Inc., USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

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PATENT FAMILY INFORMATION:

FAN 1997:511777

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				GB 1996-3242 A 19960216
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FAN 1998:479019

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FAN 2001:178434

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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
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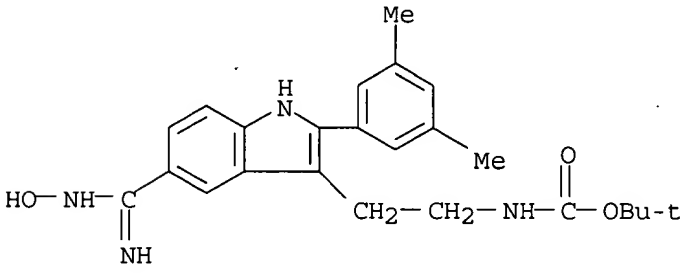
OS MARPAT 132:107953

IT **192644-10-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heterocyclic compds. as antagonists of gonadotropin releasing hormone)

RN 192644-10-3 CAPLUS

CN Carbamic acid, [2-[2-(3,5-dimethylphenyl)-5-[(hydroxyamino)iminomethyl]-1H-indol-3-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



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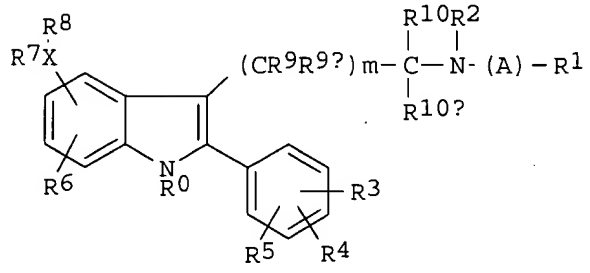

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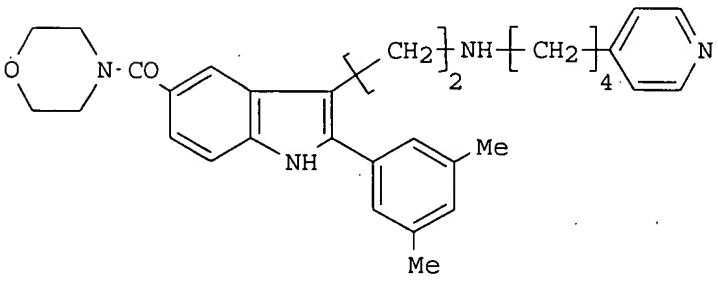

II

AB The title compds. of formula I [A = (un)substituted C1-6 alkyl, (un)substituted C3-7 cycloalkyl, (un)substituted C3-6 alkenyl, (un)substituted C3-6 alkynyl, etc; R0 = H, (un)substituted C1-6 alkyl, etc; R1 = generic heteroarom. rings with proviso given; R2 = H, (un)substituted C1-6 alkyl, (un)substituted aryl, etc; R2, A = combined

form 5-7 atom ring; R3, R4, R5 = H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, CN, NO2, C1-3 perfluoroalkyl, etc; R3, R4 = combined form ring of 3-7 carbon atoms or a heterocyclic ring contg. 1-3 heteroatoms; R6, R7 = H, (un)substituted C1-6 alkyl, etc; R8 = C(O)OR20, C(O)NR20R21, NR20R21, etc with proviso given; R7, R8 = combined form hetercyclic ring; R9, R9a = H, (un)substituted C1-6 alkyl, etc; R9, R9a = combined form carbocyclic ring of 3-7 atoms; R10, R10a = H, (un)substituted C1-6 alkyl, (un)substituted aryl, etc; R10, R10a = combined form carbocyclic ring of 3-7 atoms, double bond oxygen] useful as gonadotropin releasing hormone antagonists (no data), are prepd. For example, the title compd. II was prepd.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1997:511777 CAPLUS
DN 127:121742
TI Preparation of heterocyclic compounds as antagonists of gonadotropin releasing hormone
IN Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Girotra, Narindar N.; Lin, Peter; Wyvratt, Matthew J.
PA Merck & Co., Inc., USA; Goulet, Mark; Ashton, Wallace T.; Chu, Lin; Fisher, Michael H.; Girotra, Narindar N.; Lin, Peter; Wyvratt, Matthew J.
SO PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9721704	A1	19970619	WO 1996-US19444	19961210
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			GB 1996-3242	A 19960216
			WO 1996-US19444W	19961210
EP 873336	A1	19981028	EP 1996-944249	19961210
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PATENT FAMILY INFORMATION:

FAN 1998:479019

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FAN 2000:68450

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				WO 1999-US15581W	19990709
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				US 1998-115497 A	19980714
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	JP 2002520409	T2	20020709	JP 2000-560119	19990709

				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709

FAN 2001:178434

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6200957	B1	20010313	US 1998-115497	19980714
				US 1995-8633P P	19951214
				US 1996-760816 A2	19961205
	US 5780437	A	19980714	US 1996-760816	19961205
	JP 2001106685	A2	20010417	JP 2000-257791	19961210
				US 1995-8633P P	19951214
				GB 1996-3242 A	19960216
				JP 1997-522124 A3	19961210
	ZA 9610536	A	19970814	ZA 1996-10536	19961213
				US 1995-8633P P	19951214
	CA 2337407	AA	20000127	CA 1999-2337407	19990709
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709
	WO 2000004013	A1	20000127	WO 1999-US15581	19990709
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
				US 1998-115497 A	19980714
	AU 9949816	A1	20000207	AU 1999-49816	19990709
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709
	EP 1095038	A1	20010502	EP 1999-933850	19990709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709
	JP 2002520409	T2	20020709	JP 2000-560119	19990709
				US 1998-115497 A	19980714
				WO 1999-US15581W	19990709

OS MARPAT 127:121742

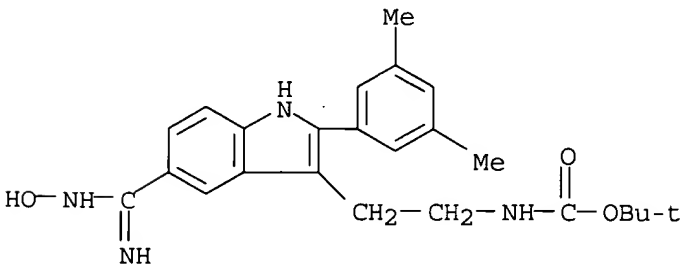
IT **192644-10-3P**

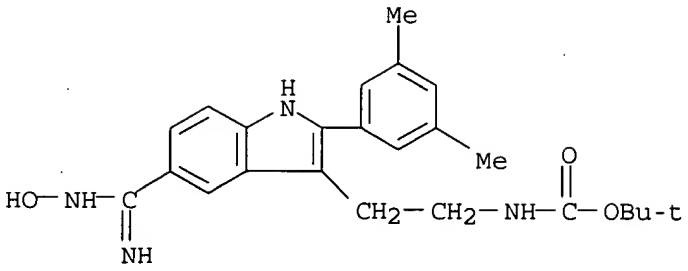
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heterocyclic compds. as antagonists of gonadotropin releasing hormone)

RN 192644-10-3 CAPLUS

CN Carbamic acid, [2-[2-(3,5-dimethylphenyl)-5-[(hydroxyamino)iminomethyl]-1H-indol-3-yl]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)





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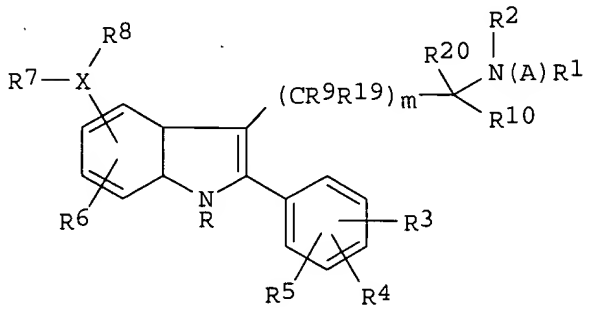
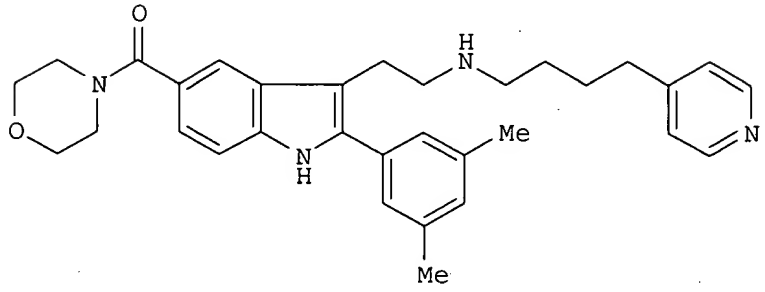


I

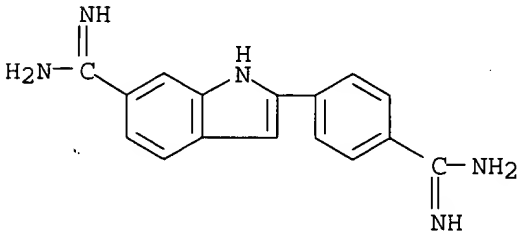


II

AB The title compds. I [A = alkyl, etc.; R = H, alkyl, etc.; R1 = heterocyclic ring (generic structures given); R2 = H, alkyl, etc.; or R2A = ring; R3, R4, R5 = H, (un)substituted alkyl, alkenyl, etc.; or R3R4 = ring; R6 = H, (un)substituted alkyl, etc.; R7 = H, (un)substituted alkyl; unless X is hydrogen or halo, then R7 is absent; R8 = heterocyclic ring, etc.; or R7R8 = heterocyclic ring; R9, R19 = H, (un)substituted alkyl; further details on R9R19 and R9A are given; R20, R10 = H, (un)substituted alkyl, etc.; further details on R20R10, and R9R20, R9R2, R20R2, R20A are given; m = 0 to 3; X = N, etc.], useful as antagonists of gonadotropin releasing hormone (no data), are prepd. I may be useful for the treatment of a variety of sex-hormone related and other conditions in both men and women. The title compd. II was prepd. in a multistep process.

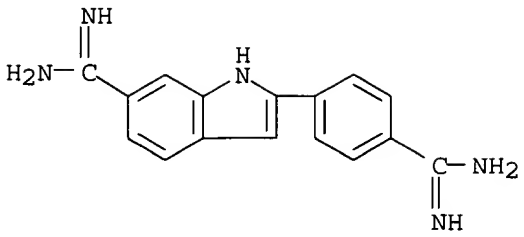
L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1994:153643 CAPLUS
DN 120:153643
TI Studies on the ability of minor groove binders to induce supercoiling in

DNA
AU Stoerl, K.; Burckhardt, G.; Lown, J. W.; Zimmer, Ch.
CS Department of Molecular Biology, Institute of Molecular Biology, Friedrich-Schiller-University, Winzerlaer Strasse 10, Jena, 07708, Germany
SO FEBS Letters (1993), 334(1), 49-54
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
IT **47165-04-8**
RL: BIOL (Biological study)
(DNA supercoiling response to)
RN 47165-04-8 CAPLUS
CN 1H-Indole-6-carboximidamide, 2-[4-(aminoiminomethyl)phenyl]- (9CI) (CA INDEX NAME)



AB The effect of various non-intercalating minor groove binders on closed circular DNA in the presence of topoisomerase I has been studied by means of agarose gel electrophoresis. Analogs of the netropsin series (lexitropsins) and SN-6999 can effectively produce pos. supercoils, as indicated by anal. of the topoisomers in the presence of chloroquine and the evaluated linking no. changes. Analogs of the distamycin series are less effective, and bisquaternary ammonium **heterocycles**, as well as DAPI and pentamidine, were found to be ineffective ligands. The large differences obsd. in the ability of minor groove binders to induce pos. supercoils are discussed.

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS
AN 1990:229384 CAPLUS
DN 112:229384
TI The interaction of unfused polyaromatic **heterocycles** with DNA: intercalation, groove-binding and bleomycin amplification
AU Wilson, W. D.; Tanious, F. A.; Barton, H. J.; Wydra, R. L.; Jones, R. L.; Boykin, D. W.; Strekowski, L.
CS Dep. Chem., Georgia State Univ., Atlanta, GA, 30303, USA
SO Anti-Cancer Drug Design (1990), 5(1), 31-42
CODEN: ACDDEA; ISSN: 0266-9536
DT Journal; General Review
LA English
IT **47165-04-8**, 4',6-Diamidino-2-phenylindole
RL: PRP (Properties)
(interaction of, with DNA, bleomycin neoplasm-inhibiting activity amplification in relation to)
RN 47165-04-8 CAPLUS
CN 1H-Indole-6-carboximidamide, 2-[4-(aminoiminomethyl)phenyl]- (9CI) (CA INDEX NAME)



AB A no. of unfused-arom. cations have been found to bind to DNA by intercalation and to amplify the bleomycin catalyzed cleavage of DNA. These mols. are more similar in structure to unfused minor-groove binding compds. such as netropsin and 4',6-diamidino-2-phenylindole (DAPI) than to fused-ring intercalators such as proflavine. An anal. of DAPI interactions with specific sequence DNA polymers has indicated that the binding modes for the mol. are sequence dependent: minor groove binding in sequences of three or more AT base pairs and intercalation in mixed or pure GC base pair sequences. As with other unfused intercalators which bind with their cationic side chains in the major groove, the amidinium groups of DAPI are in the major groove in the GC intercalation complex. DAPI is, thus, a good bleomycin amplifier in GC sequences but its minor-groove binding mode in AT sequences leads to bleomycin inhibition. Other results on bleomycin amplifiers are reviewed.

=> d cost

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
CONNECT CHARGES	0.68	2.68
NETWORK CHARGES	0.12	0.54
SEARCH CHARGES	1.64	149.39
DISPLAY CHARGES	28.78	28.78
	31.22	181.39
CAPLUS FEE (5%)	1.56	1.56
FULL ESTIMATED COST	32.78	182.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.60	-2.60

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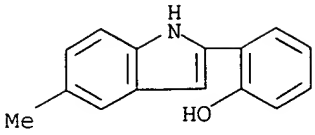
L10 ANSWER 48 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1989:85613 CAPLUS
DN 110:85613
TI Thermal recording material using chromeno compound for improved resistance to IR radiation
IN Kanda, Nobuo; Abe, Yukihiro; Kondo, Mitsuru
PA Kanzaki Paper Mfg. Co., Ltd., Japan
SO Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 273418	A2	19880706	EP 1987-119234	19871224
	EP 273418	A3	19900418		
	EP 273418	B1	19931124		
	R: DE, FR, GB				
	JP 63166588	A2	19880709	JP 1986-314744	19861227
	US 4803193	A	19890207	JP 1986-314744	19861227
				US 1987-137368	19871223
				JP 1986-314744	19861227

OS CASREACT 110:85613
IT **118234-55-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, chromeno compd. from, for thermal recording material)
RN 118234-55-2 CAPLUS
CN Phenol, 2-(5-methyl-1H-indol-2-yl)- (9CI) (CA INDEX NAME)

Patel

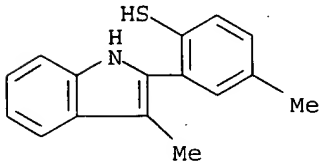
<6/13/2003>



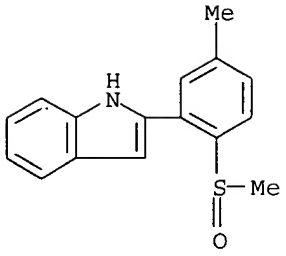
GI For diagram(s), see printed CA Issue.

AB A thermal recording material contains a colorless dye I [Z = N-contg. 5-membered ring which may have an attached benzene ring and substituents; R1-R4 = H, C1-12 alkyl, C3-C12 alkenyl or alkynyl, C5-12 cycloalkyl, Ph, Ph-C1-2 alkyl, naphthyl; R1-R4 may form a part of a **heterocycle**] and a dye developer. The developer may be selected from polyvalent metal salts of arom. carboxylic acids. The above compn. may also contain an arom. diamine compd. The compn. forms images readable by optical character-reading devices. Thus, 3,6-bis(diethylamino)fluorenone was reacted with 2-(2-hydroxyphenyl)**indole** to obtain 3,6-bis(diethylamino)spiro[fluorene-9,6'-6'-H-chromeno(4,3-b) **indole**] (II). Three different dispersions of II, 4,4'-isopropylidenediphenol, and stearic acid amide in aq. Me cellulose were mixed and used to form thermal recording papers. The papers produced images which were stable against heat, IR radiation, and humidity and ha high d.

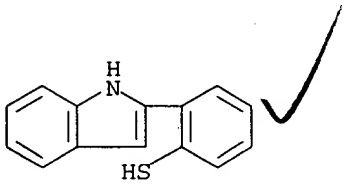
L10 ANSWER 49 OF 52 CAPLUS COPYRIGHT 2003 ACS
AN 1988:590304 CAPLUS
DN 109:190304
TI Fused **heterocycles** from o-acylbenzenethiol derivatives
AU McKinnon, David M.; Lee, Kingsley R.
CS Chem. Dep., Univ. Manitoba, Winnipeg, MB, R3T 2N2, Can.
SO Canadian Journal of Chemistry (1988), 66(6), 1405-9
CODEN: CJCHAG; ISSN: 0008-4042
DT Journal
LA English
OS CASREACT 109:190304
IT **117136-97-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and attempted cyclization of)
RN 117136-97-7 CAPLUS
CN Benzenethiol, 4-methyl-2-(3-methyl-1H-indol-2-yl)- (9CI) (CA INDEX NAME)



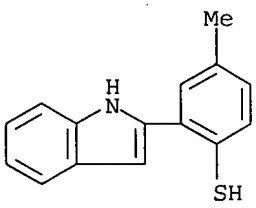
IT **117136-98-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, with hydrogen chloride)
RN 117136-98-8 CAPLUS
CN 1H-Indole, 2-[5-methyl-2-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)



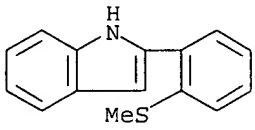
IT **117136-95-5P 117136-96-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclization of, with iodine)
RN 117136-95-5 CAPLUS
CN Benzenethiol, 2-(1H-indol-2-yl)- (9CI) (CA INDEX NAME)



RN 117136-96-6 CAPLUS
CN Benzenethiol, 2-(1H-indol-2-yl)-4-methyl- (9CI) (CA INDEX NAME)

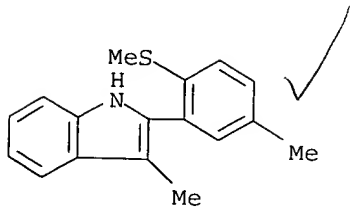


IT **117136-92-2P 117136-94-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and demethylation of, with sodium in ammonia)
RN 117136-92-2 CAPLUS
CN 1H-Indole, 2-[2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)

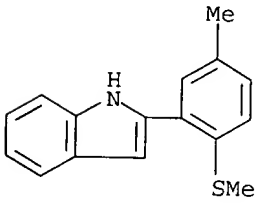


RN 117136-94-4 CAPLUS

CN 1H-Indole, 3-methyl-2-[5-methyl-2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



IT **117136-93-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn., demethylation, and S-oxidn. of)
RN 117136-93-3 CAPLUS
CN 1H-Indole, 2-[5-methyl-2-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



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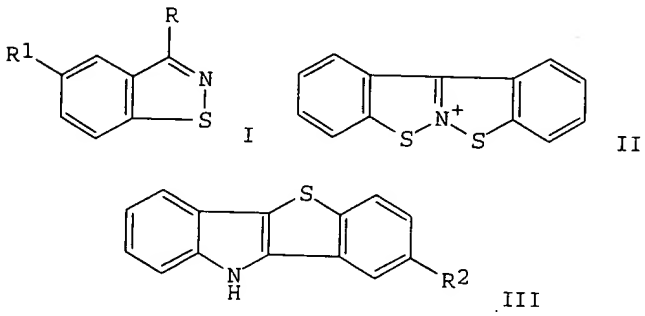

AB The oximes of 2-acylthioanisole derivs. 2,5-MeS(R1)C6H3COR (R = Me, Et, Ph, 2-MeSC6H4; R1 = H, Me) may be conveniently converted into 1,2-benzisothiazoles I Ac2O in pyridine. I (R = 2-MeSC6H4, R1 = H), prepd. by this method, was further converted into the 1,2-benzisothiazolo[2,3-b]-1,2-benzisothiazolium system II. The phenylhydrazones of certain 2-acylthioanisoles are also cyclized by polyphosphoric acid to 2-(2-methylthio)phenylindoles, which are further converted into benzo[b]thieno[3,2-b]**indoles** III (R2 = H, Me) by demethylation and oxidn.

L10 ANSWER 50 OF 52 CAPLUS COPYRIGHT 2003 ACS